Table 13: **Env**

	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species (Isotype)
679	101–342	Env( )	gp120(476–505 HAM112, O group)			Vaccine	murine(IgG2aκ)
	Vaccine:	*Vector/type:* recombinant protein	*Strain:* HAM112 (group O)	*HIV component:* gp160			
		Ab type: C-term	**References:** [Scheffel (1999)]				
	• 101–342: Overlapping peptides based on group O HAM112 Env were tested for MAb reactivity [Scheffel (1999)]						
680	101–451	Env( )	gp120(498–527 HAM112, O group)			Vaccine	murine(IgG2bκ)
	Vaccine:	*Vector/type:* recombinant protein	*Strain:* HAM112 (group O)	*HIV component:* gp160			
		Ab type: C-term	**References:** [Scheffel (1999)]				
	• 101–451: Overlapping peptides based on group O HAM112 Env were tested for MAb reactivity [Scheffel (1999)]						
681	120–1	Env( )	gp120(503–532)		no	Vaccine	murine(IgMκ)
	Vaccine:	*Vector/type:* peptide					
		Ab type: C-term	**References:** [Chanh (1986), Dalgleish (1988)]				
682	23A (2.3A)	Env(dis)	gp120(dis)		no		( )
	Ab type: C-term **Donor:** J. Robinson, Tulane University, LA **References:** [Thali (1992a), Thali (1993), Wu (1996), Trkola (1996a), Fouts (1997), Binley (1999)] • 23A: Called 2.3A – Did not block ability of gp120-sCD4 complexes to inhibit MIP-1α binding – binds to gp41-binding domain of gp120 [Wu (1996)] • 23A: C5 binding MAb – does not inhibit gp120 interaction with CCR-5 in a MIP-1β-CCR-5 competition study [Trkola (1996a)] • 23A: Study shows neutralization is not predicted by MAb binding to JRFL monomeric gp120, but is associated with oligomeric env binding – 23A bound monomer, did not bind oligomer or neutralize JRFL [Fouts (1997)] • 23A: The MAbs with the broadest neutralizing activity, IgG1b12, 2G12 and 2F5, all have high affinity for the native trimer, indicating that they were raised in an immune response to the oligomer on the virion surface rather than dissociated subunits – a disulfide linked gp120-gp41 (SOS gp140) was created to mimic the native conformation of Env and explore its potential as an immunogen – SOS gp140 is recognized by NAbs IgG1b12, 2G12, and CD4-IgG2, and also by anti-V3 MAbs 19b and 83.1 – SOSgp140 is not recognized by C4 region MAbs that neutralize only TCLA strains, G3-42 and G3-519 – nor did it bind C11, 23A, and M90, MAbs that bind to gp120 C1 and C5, where it interacts with gp41 – MAbs that bind CD4 inducible epitopes, 17b and A32 were very strongly induced by CD4 in SOS gp140 – anti-gp41 MAbs that bind in the region that interacts with gp120, 7B2, 2.2B, T4, T15G1 and 4D4, did not bind to SOSgp140, in contrast to 2F5, which binds to the only gp41 epitope that is well exposed in native gp120-gp41 complexes [Binley (1999)]					

683 D7324 Env( ) gp120( ) Vaccine sheep( )

Vaccine: *HIV component:* gp120

Ab type: C-term **Donor:** Aalto BioReagents Ltd, Dublin, Ireland
References: [Moore(1990), Sattentau & Moore(1991), Moore (1993a), Moore (1993b), Wyatt (1995), Trkola (1996a), Ditzel (1997), Ugolini (1997), Mondor (1998), Binley (1998)]

- D7324: Binding unaltered by gp120 binding to sCD4, in contrast to 110.5, 9284, 50–69 and 98–6 [Sattentau & Moore(1991)]
- D7324: Binds to the last 15 amino acids in gp120 – used for antigen capture ELISA [Wyatt (1995)]
- D7324: Epitope in C5 – Does not neutralize JR-FL nor block gp120 interaction with CCR-5 in a MIP-1β-CCR-5 competition study [Trkola (1996a)]
- D7324: Used to capture gp120 onto solid phase for epitope mapping [Moore (1993a)]
- D7324: Used to capture gp120 onto solid phase for epitope mapping [Moore (1993b)]
- D7324: Used to capture gp120 onto solid phase for epitope mapping [Ditzel (1997)]
- D7324: Used to capture gp120 onto solid phase for epitope mapping [Binley (1998)]

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684 212A Env(dis) gp120(dis) no HIV-1 infection human( )

Ab type: C1 **Donor:** J. Robinson, Tulane University, LA
References: [Robinson (1992), Moore (1994d), Moore & Sodroski(1996), Binley (1997a), Fouts (1997), Ditzel (1997), Wyatt (1997), Parren (1997b), Sullivan (1998b), Binley (1998)]

- 212A: Mutations that inhibit binding: C1 (45 W/S) and V5 (463 N/D) – and enhance binding: V2 (179/180 LD/DL) and C5 (495 G/K) [Moore (1994d)]
- 212A: Binding enhanced by anti-V3 MAb 5G11 – reciprocal inhibition with anti-C1 MAbs [Moore & Sodroski(1996)]
- 212A: Study shows neutralization is not predicted by MAb binding to JRFL monomeric gp120, but is associated with oligomeric Env binding – 212A bound monomer, did not bind oligomer or neutralize JRFL [Fouts (1997)]
- 212A: Binds efficiently to sgp120 but not soluble gp120+gp41, suggesting its gp120 epitope is blocked by gp41 binding – does not bind to HXBc2 gp120 if the 19 C-term amino acids are deleted [Wyatt (1997)]
- 212A: Does not neutralize TCLA strains or primary isolates [Parren (1997b)]
- 212A: Does not compete with binding of MAb CG10 generated in response to gp120-CD4 complex [Sullivan (1998b)]
- 212A: A panel of MAbs were shown to bind with similar or greater affinity and similar competition profiles to a deglycosylated or variable loop deleted core gp120 protein (Δ V1, V2, and V3), thus such a core protein produces a structure closely approximating full length folded monomer [Binley (1998)]

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685 522–149 Env(dis) gp120(dis) no Vaccine ( )

Vaccine: *Vector/type:* recombinant protein *HIV component:* Env

Ab type: C1 **Donor:** G. Robey, Abbott Inc.
References: [Moore & Sodroski(1996), Trkola (1996a), Binley (1998)]

- 522–149: Binding is enhanced by C5 antibodies M91 and 1C1 – mutual binding-inhibition with anti-C1 antibody 133/290 – binding is destroyed by a W/L (position 61, LAI) gp120 amino acid substitution – other C1 antibodies enhance binding to gp120 [Moore & Sodroski(1996)]

- 522–149: Does not neutralize JR-FL nor block gp120 interaction with CCR-5 in a MIP-1β-CCR-5 competition study [Trkola (1996a)]
- 522–149: A panel of MAbs were shown to bind with similar or greater affinity and similar competition profiles to a deglycosylated or variable loop deleted core gp120 protein (Δ V1, V2, and V3), thus such a core protein produces a structure closely approximating full length folded monomer [Binley (1998)]

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686 L19 Env(dis) gp120(dis HXBc2) HIV-1 infection human Fab(IgG1)

Ab type: C1 **References:** [Ditzel (1997)]

- L19: gp120 immobilized on solid phase by capture with anti-CD4 BS MAb L72 was used for the selection of Fabs – six N-term Fabs, L19 L34, L35, L52, L59, and L69, were obtained that have a similar epitope to Fab p7 [Ditzel (1997)]

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687 M90 Env(dis) gp120(dis) no Vaccine (IgG1)

Vaccine: *Vector/type:* protein *HIV component:* Env

Ab type: C1 **Donor:** Fulvia di Marzo Veronese
References: [di Marzo Veronese (1992), DeVico (1995), Moore & Sodroski(1996), Ditzel (1997), Wyatt (1997), Binley (1998), Binley (1999)]

- M90: Reactive only with native gp120, so binds to a discontinuous epitope – reacts with multiple strains [di Marzo Veronese (1992)]
- M90: Reacted with both non-reduced (but not denatured) covalently cross-linked gp120-CD4 complex [DeVico (1995)]
- M90: Reciprocal inhibition of binding of other anti-C1 MAbs – inhibits CD4 binding site MAbs – enhances binding of V2 MAbs G3-4 and SC258 [Moore & Sodroski(1996)]
- M90: Binds efficiently to sgp120 but not soluble gp120+gp41, suggesting its gp120 epitope is blocked by gp41 binding – does not bind to HXBc2 gp120 if the 19 C-term amino acids, in conjunction with C1 positions 31–82, are deleted [Wyatt (1997)]
- M90: A panel of MAbs were shown to bind with similar or greater affinity and similar competition profiles to a deglycosylated or variable loop deleted core gp120 protein (Δ V1, V2, and V3), thus such a core protein produces a structure closely approximating full length folded monomer [Binley (1998)]
- M90: The MAbs with the broadest neutralizing activity, IgG1b12, 2G12 and 2F5, all have high affinity for the native trimer, indicating that they were raised in an immune response to the oligomer on the virion surface rather than dissociated subunits – a disulfide linked gp120-gp41 (SOS gp140) was created to mimic the native conformation of Env and explore its potential as an immunogen – SOS gp140 is recognized by NAbs IgG1b12, 2G12, and CD4-IgG2, and also by anti-V3 MAbs 19b and 83.1 – SOSgp140 is not recognized by C4 region MAbs that neutralize only TCLA strains, G3-42 and G3-519 – nor did it bind C11, 23A, and M90, MAbs that bind to gp120 C1 and C5, where it interacts with gp41 – MAbs that bind CD4 inducible epitopes, 17b and A32 were very strongly induced by CD4 in SOS gp140 – anti-gp41 MAbs that bind in the region that interacts with gp120, 7B2, 2.2B, T4, T15G1 and 4D4, did not bind to SOSgp140, in contrast to 2F5, which binds to the only gp41 epitope that is well exposed in native gp120-gp41 complexes [Binley (1999)]

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688 MAG 104 Env(dis) gp120(dis) no Vaccine murine( )

Vaccine: *Vector/type:* sCD4-gp120 complex *Strain:* HXB2 *HIV component:* gp120

Ab type: C1 **Donor:** C. Y. Kang, IDEC Inc
References: [Kang (1994)]

- MAG 104: Only observed amino acid substitutions that reduce binding: 88 N/P and 106 E/A – does not bind to C1 region 20 mer peptides, tentative classification conformationally sensitive anti-C1 MAb [Kang (1994)]

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689 MAG 45 (#45) Env(dis) gp120(dis) no Vaccine murine( )

Vaccine: *Vector/type:* sCD4-gp120 complex *Strain:* HXB2 *HIV component:* gp120

Ab type: C1 **Donor:** C. Y. Kang, IDEC Inc
References: [Kang (1994), Moore & Sodroski(1996), Wyatt (1997)]

- MAG 45: Only observed amino acid substitution that reduces binding: 88 N/P – does not bind to C1 region 20 mer peptides, tentative classification conformationally sensitive anti-C1 MAb [Kang (1994)]
- MAG 45: Reciprocal binding inhibition with anti-C1-C5 and anti-C1-C4 discontinuous MAbs – binding enhanced by anti-V3 5G11 – inhibits binding of anti-CD4 binding site MAbs [Moore & Sodroski(1996)]
- MAG 45: Called #45 – binds to efficiently sgp120 but not soluble gp120+gp41, suggesting its gp120 epitope is blocked by gp41 binding – does not bind to HXBc2 gp120 if the 19 C-term amino acids, in conjunction with C1 positions 31–50, are deleted [Wyatt (1997)]

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690 MAG 95 Env(dis) gp120(dis) no Vaccine murine( )

Vaccine: *Vector/type:* sCD4-gp120 complex *Strain:* HXB2 *HIV component:* gp120

Ab type: C1 **Donor:** C. Y. Kang, IDEC Inc
References: [Kang (1994)]

- MAG 95: Only observed amino acid substitution that reduces binding: 88 N/P – does not bind to C1 region 20 mer peptides, tentative classification conformationally sensitive anti-C1 MAb [Kang (1994)]

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691 MAG 97 Env(dis) gp120(dis) no Vaccine murine( )

Vaccine: *Vector/type:* sCD4-gp120 complex *Strain:* HXB2 *HIV component:* gp120

Ab type: C1 **Donor:** C. Y. Kang, IDEC Inc
References: [Kang (1994)]

- MAG 97: Only observed amino acid substitution that reduces binding: 88 N/P – does not bind to C1 region 20 mer peptides, tentative classification conformationally sensitive anti-C1 MAb [Kang (1994)]

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692 p7 Env(dis) gp120(dis HXBc2) no HIV-1 infection human Fab(IgG1)

Ab type: C1 **References:** [Ditzel (1997), Parren (1997b)]

- p7: gp120 immobilized on solid phase by capture with sCD4 was used for selection of Fabs – three novel N-term Fabs were obtained that bind to similar epitopes, p7, p20, and p35 – a C1 W/S substitution at position 45 abolished binding, a Y/D at position 45 reduced binding, and C5 region substitutions 475 M/S and 493 P/K enhanced binding – compete with MAbs M85, M90 and 212A, but not M91 and G3-299 [Ditzel (1997)]
- p7: Does not neutralize TCLA strains or primary isolates [Parren (1997b)]

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693 L100 | Env(dis) | gp120(dis HXBc2) | | HIV-1 infection | human Fab(IgG1)

Ab type: C1-C2 **References:** [Ditzel (1997), Parren (1997b), Parren & Burton(1997)]

- L100: Does not neutralize TCLA strains or primary isolates [Parren (1997b)]
- L100: gp120 immobilized on solid phase by capture with sCD4 and then masked with Fab p7 allowed selection of a new Fab, L100, with a novel specificity for C1 and C2 – gp120 C1 substitutions 69 W/L and 76 P/Y abolish L100 binding, and C2 substitutions 252 R/W, 256 S/Y, 262 N/T and 267 E/L abolish or strongly inhibit L100 binding – inhibits binding of MAbs M90 and G3-299, but not M85, 212A, and M91 [Ditzel (1997), Parren & Burton(1997)]

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694 2/11c (211c, 2.11c, 211/c, 2–11c) | Env(dis) | gp120(dis) | L (weak) | HIV-1 infection | human( )

Ab type: C1-C4 **Donor:** J. Robinson, Tulane University, LA
References: [Moore & Sodroski(1996), Trkola (1996a), Binley (1997a), Fouts (1997), Li (1997), Wyatt (1997), Binley (1998)]

- 2/11c: Inhibits binding of anti-C1, -C5, -C4, -V3 and anti-CD4 binding site MAbs – induces binding of some anti-V2 and CD4i MAbs (48d and 17b) – similar reactivity pattern to A32, but less cross-reactive and lower affinity – A32 and 211/c are unique among known human and rodent MAbs [Moore & Sodroski(1996)]
- 2/11c: Called 211c – does not neutralize JR-FL nor block gp120 interaction with CCR-5 in a MIP-1β-CCR-5 competition study [Trkola (1996a)]
- 2/11c: Study shows neutralization is not predicted by MAb binding to JRFL monomeric gp120, but is associated with oligomeric env binding – 2/11c bound monomer, did not bind oligomer or neutralize JRFL [Fouts (1997)]
- 2/11c: Called 2.11c – One of 14 human MAbs tested for ability to neutralize a chimeric SHIV-vpu+, which expressed HIV-1 IIIB env – 50% neutralization could not be achieved at a maximal concentration of 67 μg/ml [Li (1997)]
- 2/11c: Binds efficiently to sgp120 but not soluble gp120+gp41, suggesting its gp120 epitope is blocked by gp41 binding – does not bind to HXBc2 gp120 if the 19 C-term amino acids, in conjunction with C1 positions 31–74, are deleted [Wyatt (1997)]
- 2/11c: Called 211/c – a panel of MAbs were shown to bind with similar or greater affinity and similar competition profiles to a deglycosylated or variable loop deleted core gp120 protein (Δ V1, V2, and V3), thus such a core protein produces a structure closely approximating full length folded monomer [Binley (1998)]

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695 C11 (c11) | Env(dis) | gp120(dis) | no | HIV-1 infection | human( )

Ab type: C1-C5 **Donor:** J. Robinson, Tulane University, LA
References: [Robinson (1992), Moore (1994d), Moore & Sodroski(1996), Trkola (1996a), Wu (1996), Binley (1997a), Fouts (1997), Wyatt (1997), Parren (1997b), Sullivan (1998b), Binley (1999)]

- C11: Mutations that inhibit binding: C1 (45 W/S, 88 N/P) – V5 (463 N/D) – and C5 (491 I/F, 493 P/K and 495 G/K) and enhance binding: C1 (36 V/L) – V1-V2 (152/153 GE/SM) – and ΔV1/V2/V3 [Moore (1994d)]
- C11: Binding enhanced by anti-V3 MAb 5G11 – reciprocal inhibition with anti-C1 MAbs [Moore & Sodroski(1996)]
- C11: Did not block ability of gp120-sCD4 complexes to inhibit MIP-1α binding – binds to gp41-binding domain [Wu (1996)]
- C11: Does not neutralize JR-FL nor block gp120 interaction with CCR-5 in a MIP-1β-CCR-5 competition study [Trkola (1996a)]

- C11: Study shows neutralization is not predicted by MAb binding to JRFL monomeric gp120, but is associated with oligomeric Env binding – C11 bound monomer, did not bind oligomer or neutralize JRFL [Fouts (1997)]
- C11: Binds efficiently to sgp120 but not soluble gp120+gp41, suggesting its gp120 epitope is blocked by gp41 binding – partial reexposure if sCD4 was bound – does not bind to HXBc2 gp120 if the 19 C-term amino acids are deleted [Wyatt (1997)]
- C11: Does not neutralize TCLA strains or primary isolates [Parren (1997b)]
- C11: Does not compete with binding of MAb generated in response to gp120-CD4 complex, CG10 [Sullivan (1998b)]
- C11: The MAbs with the broadest neutralizing activity, IgG1b12, 2G12 and 2F5, all have high affinity for the native trimer, indicating that they were raised in an immune response to the oligomer on the virion surface rather than dissociated subunits – a disulfide linked gp120-gp41 (SOS gp140) was created to mimic the native conformation of Env and explore its potential as an immunogen – SOS gp140 is recognized by NAbs IgG1b12, 2G12, and CD4-IgG2, and also by anti-V3 MAbs 19b and 83.1 – SOSgp140 is not recognized by C4 region MAbs that neutralize only TCLA strains, G3-42 and G3-519 – nor did it bind C11, 23A, and M90, MAbs that bind to gp120 C1 and C5, where it interacts with gp41 – MAbs that bind CD4 inducible epitopes, 17b and A32 were very strongly induced by CD4 in SOS gp140 – anti-gp41 MAbs that bind in the region that interacts with gp120, 7B2, 2.2B, T4, T15G1 and 4D4, did not bind to SOSgp140, in contrast to 2F5, which binds to the only gp41 epitope that is well exposed in native gp120-gp41 complexes [Binley (1999)]

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696 L81 Env(dis) gp120(dis) no HIV-1 infection human(IgG1)

Ab type: C1-C5 **References:** [Ditzel (1997), Parren (1997b)]

- L81: gp120 immobilized on solid phase by capture with anti-CD4 BS MAb L72 was used for selection of Fabs – L81 binding is abolished by C1 substitution 45 W/S, C5 substitution 491 I/F, and C3 substitution L/A [Ditzel (1997)]
- L81: Does not neutralize TCLA strains or primary isolates [Parren (1997b)]

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697 2F19C Env( ) gp120(HIV2ROD) APGK no Vaccine murine( )

Vaccine: *Vector/type:* peptide *Strain:* HIV-2 ROD

Ab type: C3 **References:** [Matsushita (1995)]

- 2F19C: Binds in WB, but binds poorly to Env on the cell surface, APGK is the core binding region [Matsushita (1995)]

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698 B2C Env( ) gp120(HIV2ROD) HYQ(core) L Vaccine murine( )

Vaccine: *Vector/type:* peptide *Strain:* HIV-2 ROD

Ab type: C3 **References:** [Matsushita (1995)]

- B2C: Viral neutralization was type-specific for HIV-2 ROD [Matsushita (1995)]

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699 1024 Env( ) gp120( ) ( )

Ab type: C4 **References:** [Berman (1997)]

- 1024: Binds to 1/7 isolates from breakthrough cases from a MN gp120 vaccine trial [Berman (1997)]

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700 10/46c Env(dis) gp120(dis) Vaccine rat( )

Vaccine: *Vector/type:* recombinant protein *HIV component:* gp120

Ab type: CD4BS **References:** [Cordell (1991), Jeffs (1996), Peet (1998)]

- 10/46c: Increased binding when V1/V2 or V1/V2 and V3 were deleted from gp120 [Jeffs (1996)]
- 10/46c: The most variable amino acids in the V3 loop were replaced with serines to make the immunodominant V3 loop less immunogenic – these changes did not affect the ability of sCD4 or MAbs to V1/V2, C1 and C4 to bind – 10/46c was not affected by V3 serine substitutions – mice injected with serine substituted gp120 had a reduced response relative to wildtype, and no enhanced immunogenicity of conserved regions [Peet (1998)]

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701 1027–30-D Env(dis) Env(dis) human(IgG1κ)

Ab type: CD4BS **Donor:** Susan Zolla-Pazner (Zollas01@mcrcr6.med.nyu) (NYU Med. Center)

References: [Hioe (2000)]

- 1027–30-D: Ab responses, because of their capacity to alter antigen uptake and processing, can influence helper T cell responses – anti-CD4 binding site MAbs or serum Ig from HIV+ individuals inihibited proliferative responses of gp120 specific T cells – CD4BS MAbs 654-D, 559/64-D, 588-D, 830-D, 1027–30-D, and 1202–30D strongly diminished proliferation [Hioe (2000)]

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702 1125H (1125h) Env(dis) gp120(dis) L (MN) HIV-1 infection human(IgG1κ)

Ab type: CD4BS **Donor:** Shermaine Tilley, Public Health Research Institute, USA

References: [Tilley (1991b), Tilley (1991a), Thali (1992a), Wyatt (1992), Pinter (1993b), D'Souza (1995), Warrier (1996), Pincus (1996), Wyatt (1998), Alsmadi & Tilley(1998), Yang (1998)]

- 1125H: Binding to gp120 inhibited by CD4 – epitope is destroyed by reduction, but not by removal of N-linked sugars – potent neutralization of MN, RF, SF-2 and IIIB – neutralization synergy with anti-V3 MAb 4117C [Tilley (1991a)]
- 1125H: Amino acid substitutions in HXB2 that strongly inhibit binding: 88, 102, 117, 113, 257, 368, 370, 421, 427, 457, 470, 480 [Thali (1992a)]
- 1125H: Binding to soluble gp120 enhanced by the presence of an anti-V3 HuMAb, 41148D [Pinter (1993b)]
- 1125H: Precipitation of Δ 297–329 env glycoprotein, with has a deleted V3 loop, is much more efficient that precipitation of wild type [Wyatt (1992)]
- 1125H: Neutralization was MN specific – failed to neutralize JRCSF, and 2 B subtype and 1 D subtype primary isolates in a multi-laboratory study involving 11 labs [D'Souza (1995)]
- 1125H: Synergistic neutralization of HIV-1 when combined with anti-V2 MAb C108G [Warrier (1996)]
- 1125H: A panel of immunotoxins were generated by linking Env MAbs to ricin A – immunotoxins mediated cell killing, but killing was not directly proportional to binding [Pincus (1996)]
- 1125H: Called 1125h – summary of the implications of the crystal structure of the core of gp120 bound to CD4 and 17b with what is known about mutations that reduce NAb binding – probable mechanism of neutralization by CD4BS Ab is direct interference with CD4 binding [Wyatt (1998)]
- 1125H: A study of 6 anti-Env MAbs and their ability to bind or direct ADCC against target cells infected with IIIB, MN, SF-2, and RF – bound and directed lysis against all four strains [Alsmadi & Tilley(1998)]
- 1125H: A neutralization assay was developed based on hemi-nested PCR amplification of the LTR (HNPCR) – LTR-HNPCR consistently revealed HIV DNA and was shown to be a rapid, specific and reliable neutralization assay based on tests with 6 MAbs and 5 isolates [Yang (1998)]

703	120–1B1	Env(dis)	gp120(dis)	L	human( )

Ab type: CD4BS **Donor:** Virus Testing Systems Corp., Houston, TX
References: [Watkins (1993)]

- 120–1B1: A neutralization escape mutant (HXB2 A281V) was selected by growth of HXB2 in the presence of broadly neutralizing sera – 120–1B1 was not affected by this mutation [Watkins (1993)]

704	1202-D (1202–30-D)	Env(dis)	Env(dis)		human(IgG1κ)

Ab type: CD4BS **Donor:** Susan Zolla-Pazner (Zollas01@mcrcr6.med.nyu) (NYU Med. Center)
References: [Nyambi (1998), Hioe (2000), Nyambi (2000)]

- 1202-D: Using a whole virion-ELISA method, 18 human MAbs were tested for their ability to bind to a panel of 9 viruses from clades A, B, D, F, G, and H – CD4-BS Abs tended to bind weakly without clade specificity to virions, but bound well to soluble gp120 – 1202-D did not bind to any B clade viruses, and weakly bound A, C, and G clade isolates – 559/64-D, 558-D and 1202-D had similar reactivities [Nyambi (1998)]
- 1202-D: Called 1202–30D – Ab responses, because of their capacity to alter antigen uptake and processing, can influence helper T cell responses – anti-CD4 binding site MAbs or serum Ig from HIV+ individuals inihibited proliferative responses of gp120 specific T cells – CD4BS MAbs 654-D, 559/64-D, 588-D, 830-D, 1027–30-D, and 1202–30D strongly diminished proliferation [Hioe (2000)]
- 1202-D: 26 HIV-1 group M isolates (clades A to H) were tested for binding to 47 MAbs, including 6 CD4BS MAbs – CD4BS MAbs bound consistently to most isolates of clade D, but poorly to isolates of other clades with the exception of broadly reactive MAb IgG1b12[Nyambi (2000)]

705	1331E	Env(dis)	gp120(dis IIIB)	HIV-1 infection	human(IgG1κ)

Ab type: CD4BS **Donor:** Susan Zolla-Pazner (Zollas01@mcrcr6.med.nyu) (NYU Med. Center)
References: [Gorny (2000)]

- 1331E: Inhibits sCD4 binding to rec gp120 LAI – binding of panel of 21 MAbs to soluble oligomeric gp140 versus gp41 or gp120 monomers was compared – no MAb was oligomer specific, though anti-V3 and CD4BS MAbs reacted better with the oligomer and V2 and C5 tended to favor the monomer – CD4BS MAbs 559/64-D, 654-D, 729-D, 9CL and 1331E bound with a 5–13 fold preference for the oligomer [Gorny (2000)]

706	1570 (1570A, 1570C, and 1570D)	Env(dis)	Env(dis PR12, BH10 core)	HIV-1 infection	human( )

Ab type: CD4BS **References:** [Jeffs (2001)]

- 1570: BH10 was mutated to form the PR12 protein with the first 74 C-terminal amino acids and the V1, V2 and V3 hypervariable loops deleted and a very well exposed CD4 binding domain (CD4bd) – this proteins was used to select three new human CD4BS MAbs 1570, 1595 and 1599 – three MAbs were isolated from one individual, 1570A, C and D but all were determined to have the same V(H)3 region – 1570 was able to bind to a panel of recombinant proteins from the A, B, C, D, and E subtypes [Jeffs (2001)]

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707 1595 Env(dis) Env(dis PR12, BH10 core) HIV-1 infection human( )

Ab type: CD4BS **References:** [Jeffs (2001)]

- 1595: BH10 was mutated to form the PR12 protein with the first 74 C-terminal amino acids and the V1, V2 and V3 hypervariable loops deleted and a very well exposed CD4 binding domain (CD4bd) – this proteins was used to select three new human CD4BS MAbs 1570, 1595 and 1599 – 1595 was able to bind gp120 from the A, B, and D clades from a panel of recombinant proteins from the A, B, C, D, and E subtypes [Jeffs (2001)]

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708 1599 Env(dis) Env(dis PR12, BH10 core) HIV-1 infection human( )

Ab type: CD4BS **References:** [Jeffs (2001)]

- 1599: BH10 was mutated to form the PR12 protein with the first 74 C-terminal amino acids and the V1, V2 and V3 hypervariable loops deleted and a very well exposed CD4 binding domain (CD4bd) – this proteins was used to select three new human CD4BS MAbs 1570, 1595 and 1599 – 1599 was able to bind gp120 only from the B clade from a panel of recombinant proteins from the A, B, C, D, and E subtypes [Jeffs (2001)]

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709 15e (1.5e, 1.5E, 15E) Env(dis) gp120(dis) L HIV-1 infection human(IgG1κ)

Ab type: CD4BS **Donor:** J. Robinson, Tulane University, LA, and David Ho, ADARC, NY, NY
References: [Robinson (1990a), Thali (1991), Cordell (1991), Ho (1991b), Koup (1991), Ho (1992), Wyatt (1992), Thali (1992a), Takeda (1992), Moore & Ho(1993), Thali (1993), Wyatt (1993), Bagley (1994), Thali (1994), Cook (1994), Moore (1994b), Moore (1994a), Sattentau & Moore(1995), Lee (1995), McKeating (1996), Moore & Sodroski(1996), Poignard (1996a), Trkola (1996a), McDougal (1996), Wisnewski (1996), Binley (1997a), Fouts (1997), Li (1997), Wyatt (1997), Berman (1997), Parren (1997b), Wyatt (1998), Parren (1998a), Sullivan (1998b), Binley (1998), Trkola (1998), Fouts (1998), Sullivan (1998a), Park (2000), Kolchinsky (2001)]

- 15e: Broadly neutralizing, binds multiple strains, competes with CD4 for gp120 binding, DTT reduction of env abrogates binding – more potent blocking of gp120-sCD4 binding than MAbs G3-536 and G3-537 [Ho (1991b)]
- 15e: Cross-competes with MAbs ICR 39.13g and ICR 39.3b [Cordell (1991)]
- 15e: Binds to gp120 of HIV-1 IIIB, but not RF – mediates ADCC – deletion of the V3 loop from gp120 does not alter ADCC activity [Koup (1991)]
- 15e: gp120 mutants that affect 15e epitope binding: 113, 257, 368, 370, 421, 427, 475 – four of these coincide with amino acids important for the CD4 binding domain [Ho (1992)]
- 15e: Precipitation of Δ 297–329 env glycoprotein, with a deleted V3 loop, is much more efficient that precipitation of wild type [Wyatt (1992)]
- 15e: Amino acid substitutions in HXB2 that strongly inhibit binding, similar to [Ho (1992)], some additional, 88, 102, 117, 113, 257, 368, 370, 421, 427, 457, 470, 480 [Thali (1992a)]
- 15e: Called N70–1.5e – does not enhance infection of HIV-1 IIIB and MN [Thali (1992a)]
- 15e: Conformational, does not bind denatured gp120 – neutralizes IIIB – reactive with SF-2 gp120 – strong inhibition of HIV+ human sera binding to IIIB gp120 [Moore & Ho(1993)]

- 15e: Binding to Δ V1/2 and Δ V1/2/3 mutant glycoproteins is greater than binding to wildtype gp120 [Wyatt (1993)]
- 15e: Called 15E – a neutralization escape mutant (HXB2 A281V) was selected by growth of HXB2 in the presence of broadly neutralizing sera – 15E neutralization was not affected by this mutation [Watkins (1993)]
- 15e: Heavy chain is V HIV, V2–1 – light chain is V_kappaI, Hum01/012. Compared to 21h and F105 [Bagley (1994)]
- 15e: A mutation in gp41, 582 A/T, confers resistance to neutralization (also confers resistance to MAbs F105, 48d, 21h and 17b) [Thali (1994)]
- 15e: MAbs against the glycosphingolipid GalCer block HIV infection of normally susceptible CD4 negative cells from the brain and colon – anti-CD4 MAbs moderately inhibit gp120 binding to GalCer, possibly through steric hindrance – binding of GalCer to gp120 inhibited but did not completely block 15e binding [Cook (1994)]
- 15e: Cross-reactive with gp120 proteins from clades B and D, less so with A and C, and not reactive with clade E and F [Moore (1994b)]
- 15e: Binds with higher affinity to monomer than to oligomer, moderate association rate [Sattentau & Moore(1995)]
- 15e: The V4 and V5 domains are essential for 1.5e binding, in contrast to the V1, V2, and V3 loops [Lee (1995)]
- 15e: Called 1.5e – Neutralizes HXB2, but fails to neutralize chimeric virus with gp120 from primary isolates in an HXB2 background [McKeating (1996)]
- 15e: gp120 binding enhanced by anti-V3 MAb 5G11 and anti-V2 MAb G3-136 – binding inhibited by other CD4 binding site MAbs, antibodies that bind to gp120 only when CD4 is bound, and CD4-IgG [Moore & Sodroski(1996)]
- 15e: Anti-CD4BS MAbs 15e, 21h, and IgG1b12 did not cause gp120 dissociation from virus, or exposure of the gp41 epitope of MAb 50–69, in contrast to CD4i MAb 48d and anti-V3 neutralizing MAbs [Poignard (1996a)]
- 15e: Inhibits gp120 interaction with CCR-5 in a MIP-1β-CCR-5 competition study [Trkola (1996a)]
- 15e: Neutralizes HIV-1 LAI less potently than V3 specific MAbs [McDougal (1996)]
- 15e: 15e is V H4 – V-region heavy chain usage was examined and a bias of enhanced V H1 and V H4, and reduced V H3, was noted among HIV infected individuals [Wisnewski (1996)]
- 15e: Study shows neutralization is not predicted by MAb binding to JRFL monomeric gp120, but is associated with oligomeric Env binding – 15e bound monomer, did not bind oligomer or neutralize JRFL [Fouts (1997)]
- 15e: One of 14 human MAbs tested for ability to neutralize a chimeric SHIV-vpu+, which expressed HIV-1 IIIB env – 15e could only achieve 50% neutralization, but could act synergistically with anti-V3 MAb 694/98-D to achieve 90% [Li (1997)]
- 15e: Does not bind to HXBc2 gp120 if the 19 C-term amino acids, in conjunction with C1 positions 31–93, are deleted [Wyatt (1997)]
- 15e: Called 1.5E – Binds to 7/7 isolates from breakthrough cases from a MN gp120 vaccine trial [Berman (1997)]
- 15e: Neutralizes TCLA strains, but not primary isolates [Parren (1997b)]
- 15e: Summary of the implications of the crystal structure of the core of gp120 bound to CD4 and 17b with what is known about mutations that reduce NAb binding – probable mechanism of neutralization by CD4BS Ab is direct interference with CD4 binding [Wyatt (1998)]
- 15e: The MAb and Fab binding to the oligomeric form of gp120 and neutralization were highly correlated – authors suggest that neutralization is determined by the fraction of Ab sites occupied on a virion irrespective of the epitope [Parren (1998a)]

- 15e: A panel of MAbs were shown to bind with similar or greater affinity and similar competition profiles to a deglycosylated or variable loop deleted core gp120 protein (Δ V1, V2, and V3), thus such a core protein produces a structure closely approximating full length folded monomer – CD4BS MAbs 15e, F91 and IgG1b12 bound better to the deleted protein than to wild type [Binley (1998)]
- 15e: Competes with CG-10 binding, a MAb raised against a gp120 CD4 complex, this was probably due to the disruption of CD4-gp120 by 15e [Sullivan (1998b)]
- 15e: No detectable neutralizing activity among primary isolates with different co-receptor usage – some neutralization of TCLA strains [Trkola (1998)]
- 15e: CD4BS MAbs 15e, 21h, and F91 bind with even lower affinity than 205-43-1 and 205-42-15 to JRFL oligomer [Fouts (1998)]
- 15e: Called 1.5e – the HIV-1 virus YU2 entry can be enhanced by MAbs binding to the CD4BS, V3 loop, and CD4i epitopes – the activation for this enhanced entry state could be conferred on HxB2 by introducing the YU2 V3 loop, or the YU2 V3 and V1/V2 loops – a similar effect is observed by sub-neutralizing concentrations of sCD4 and the effect is dependent of CCR5 – 1.5e enhances and does not neutralize YU2 env even at 50 μg/ml [Sullivan (1998a)]
- 15e: Six mutations in MN change the virus from a high-infectivity neutralization resistant phenotype to low-infectivity neutralization sensitive – V3, CD4BS, and CD4i MAbs are 20–100 fold more efficient at neutralizing the sensitive form – the mutation L544P reduced binding of all MAbs against gp120 by causing conformational changes [Park (2000)]
- 15e: Mutations in two glcosylation sites in the V2 region of HIV-1 ADA at positions 190 and 197 (187 DNTSYRLINCNTS 199) cause the virus to become CD4-independent and able to enter cells through CCR5 alone – these same mutations tended to increase the neutralization sensitivity of the virus, including to 15e [Kolchinsky (2001)]
- 15e: UK Medical Research Council AIDS reagent: ARP3016

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710 205-43-1 Env(dis) gp120(dis) no HIV-1 infection human( )

Ab type: CD4BS **References:** [Fouts (1998), Grovit-Ferbas (2000)]

- 205-43-1: Rank order of CD4BS antibodies oligomer binding is IgG1b12 = 2G6 = 205-46-9 > 205-43-1 = 205-42-15 > 15e = 21h = F91, and the only thing notably distinguishing about neutralizing IgG1b12 is that it depends on residues in V2 [Fouts (1998)]
- 205-43-1: To determine the antigenicity of virus killed by thermal and chemical inactivation, retention of conformation-dependent neutralization epitopes was examined, and exposure of CD4BS epitopes was found to be enhanced (MAbs IgG1b12, 205-46-9, and 205-43-1) – binding to 2G12 and 447-52D epitopes was essentially unaltered – the 17b CD4i epitope was also exposed [Grovit-Ferbas (2000)]

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711 205-46-9 Env(dis) gp120(dis) no HIV-1 infection human( )

Ab type: CD4BS **References:** [Fouts (1998), Grovit-Ferbas (2000)]

- 205-46-9: Binds JRSF oligomer with high affinity as does IgG1b12, but IgG1b12 is neutralizing, 205-46-9 is not – conclusions of this paper contrast with Parren98 – authors propose a model where 205-46-9 and 2G6 may inhibit CD4 binding, but cause a conformational shift which enhances CCR5 binding and thus counteracts the neutralizing effect – rank order of CD4BS antibodies oligomer binding is IgG1b12 = 2G6 = 205-46-9 > 205-43-1 = 205-42-15 > 15e = 21h = F91, and the only thing notably distinguishing about neutralizing IgG1b12 is that it depends on residues in V2 [Fouts (1998)]

- 205-46-9: To determine the antigenicity of virus killed by thermal and chemical inactivation, retention of conformation-dependent neutralization epitopes was examined, and exposure of CD4BS epitopes was found to be enhanced (MAbs IgG1b12, 205-46-9, and 205-43-1) – binding to 2G12 and 447-52D epitopes was essentially unaltered – the 17b CD4i epitope was also exposed [Grovit-Ferbas (2000)]

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712 21h (2.1H) Env(dis) gp120(dis) L HIV-1 infection human(IgG1)

Ab type: CD4BS **Donor:** J. Robinson, Tulane University, LA

References: [Ho (1991b), Thali (1992a), Ho (1992), Wyatt (1993), Moore & Ho(1993), Moore (1994b), Moore (1994a), Bagley (1994), Thali (1994), Sattentau & Moore(1995), Moore & Sodroski(1996), Poignard (1996a), Wisnewski (1996), McKeating (1996), Binley (1997a), Fouts (1997), Li (1997), Ugolini (1997), Wyatt (1997), Parren (1997b), Wyatt (1998), Parren (1998a), Fouts (1998)]

- 21h: Amino acid substitutions in HXB2 that inhibit binding, some shared with CD4 binding inhibition, 88, 113, 257, 368, 370, 421, 470, 480 [Thali (1992a)]
- 21h: Binding to Δ V1/2 and Δ V1/2/3 mutant glycoproteins is greater than binding to wildtype gp120 [Wyatt (1993)]
- 21h: Conformational, does not bind denatured gp120 – neutralizes IIIB – reactive with SF-2 gp120 – strong inhibition of HIV+ human sera binding to IIIB gp120 [Moore & Ho(1993)]
- 21h: Has strong cross-reactivity with gp120 monomers from most subtypes, A-F, with the least reactivity to clade E [Moore (1994b)]
- 21h: Competition studies with human sera from seroconverting individuals showed that anti-CD4 BS antibodies can arise very early in infection, comparable or prior to anti-V3 antibodies [Moore (1994a)]
- 21h: Heavy chain is V HIII, VDP-35 – light chain is V_lambdaIIIa, Hum318. Compared to 15e and F105 [Bagley (1994)]
- 21h: A mutation in gp41, 582 A/T, confers resistance to neutralization (also confers resistance to MAbs F105, 48d, 15e and 17b) [Thali (1994)]
- 21h: Binds with higher affinity to monomer than to oligomer, moderate association rate [Sattentau & Moore(1995)]
- 21h: Anti-CD4 binding site MAb – reciprocal inhibition by anti-C1, -C4 and other anti-CD4 binding site antibodies – enhanced by some anti-V2 MAbs and anti-V3 MAb 5G11 – enhances binding of some anti-V3 and -V2 MAbs [Moore & Sodroski(1996)]
- 21h: Anti-CD4BS MAbs 15e, 21h, and IgG1b12 did not cause gp120 dissociation from virus, or exposure of the gp41 epitope of MAb 50–69, in contrast to CD4i MAb 48d and anti-V3 neutralizing MAbs [Poignard (1996a)]
- 21h: 21h is V H3 – V-region heavy chain usage was examined and a bias of enhanced V H1 and V H4, and reduced V H3, was noted among HIV infected individuals [Wisnewski (1996)]
- 21h: Called 2.1H – Neutralizes HXB2, but fails to neutralize chimeric virus with gp120 from primary isolates in an HXB2 background [McKeating (1996)]
- 21h: Study shows neutralization is not predicted by MAb binding to JRFL monomeric gp120, but is associated with oligomeric Env binding – 21h bound monomer, did not bind oligomer or neutralize JRFL [Fouts (1997)]
- 21h: One of 14 human MAbs tested for ability to neutralize a chimeric SHIV-vpu+, which expressed HIV-1 IIIB env – 50% neutralization could not be achieved at a maximal concentration of 67 μg/ml [Li (1997)]
- 21h: Viral binding inhibition by 21h strongly correlated with neutralization (all other neutralizing MAbs tested showed some correlation except 2F5) [Ugolini (1997)]

- 21h: Binds both gp120 and soluble gp120+gp41 complex efficiently, suggesting its gp120 epitope is not blocked by gp41 binding – major deletions in C1 and C5 and deletions of the V1V2 and V3 loops do not diminish binding [Wyatt (1997)]
- 21h: Neutralizes TCLA strains, but not primary isolates [Parren (1997b)]
- 21h: Summary of the implications of the crystal structure of the core of gp120 bound to CD4 and 17b with what is known about mutations that reduce NAb binding – probable mechanism of neutralization by CD4BS Ab is direct interference with CD4 binding [Wyatt (1998)]
- 21h: The MAb and Fab binding to the oligomeric form of gp120 and neutralization were highly correlated – authors suggest that neutralization is determined by the fraction of Ab sites occupied on a virion irrespective of the epitope [Parren (1998a)]
- 21h: CD4BS MAbs 15e, 21h, and F91 bind with even lower affinity than 205-43-1 and 205-42-15 to JRFL oligomer – conclusions of this paper contrast with [Parren (1998a)] [Fouts (1998)]
- 21h: UK Medical Research Council AIDS reagent: ARP3017

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713 2G6 Env(dis) gp120(dis) ( )

Ab type: CD4BS **Donor:** Herman Katinger, Inst. Appl. Microbiol. University of Agricultural Science, or Polymun Scientific Inc., Vienna, Austria
References: [Fouts (1998)]

- 2G6: Binds to JRFL oligomer with an affinity comparable to IgG1b12, but does not neutralize the virus, so binding of oligomer is not always predictive of neutralization – conclusions of this paper contrast with [Parren (1998a)] – authors propose a model where 205-46-9 and 2G6 may inhibit CD4 binding, but cause a conformational shift which enhances CCR5 binding and thus counteracts the neutralizing effect [Fouts (1998)]

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714 428 Env(dis) gp120(dis) HIV-1 infection human( )

Ab type: CD4BS **References:** [Karwowska (1992a), Jeffs (1996)]

- 428: Slight, not significant increased binding when V1/V2 or V1/V2 and V3 were deleted from gp120 [Jeffs (1996)]

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715 448-D (448D) Env(dis) gp120(dis) L HIV-1 infection human(IgG1λ)

Ab type: CD4BS **Donor:** Susan Zolla-Pazner (Zollas01@mcrcr6.med.nyu), NYU Med Center, NY, NY
References: [Karwowska (1992a), McKeating (1992c), Spear (1993), Laal (1994), Forthal (1995), Manca (1995), Li (1997), Wyatt (1998), Nyambi (2000)]

- 448-D: Conformational – reactive with IIIB gp120 in RIP, but not WB assay [Karwowska (1992a)]
- 448-D: Called 448D – blocks gp120-CD4 binding – substitutions at gp120 residues 88, 113, 117, 257, 368 and 370 reduce binding – epitope similar to rat MAbs 39.13g and 39.3b [McKeating (1992c)]
- 448-D: Did not mediate deposition of complement component C3 on HIV infected cells [Spear (1993)]
- 448-D: Dissociation constant gp120 IIIB 0.029 – neutralizes IIIB, acts synergistically with anti-V3 MAb 447-52D [Laal (1994)]
- 448-D: Neutralizing activity, positive ADCC activity, and no viral enhancing activity [Forthal (1995)]
- 448-D: Virions complexed to gp120 Ab facilitate presentation of p66 RT epitopes to Th cells [Manca (1995)]
- 448-D: One of 14 human MAbs tested for ability to neutralize a chimeric SHIV-vpu+, which expressed HIV-1 IIIB env [Li (1997)]

- 448-D: Summary of the implications of the crystal structure of the core of gp120 bound to CD4 and 17b with what is known about mutations that reduce NAb binding – probable mechanism of neutralization by CD4BS Ab is direct interference with CD4 binding [Wyatt (1998)]
- 448-D: 26 HIV-1 group M isolates (clades A to H) were tested for binding to 47 MAbs, including 6 CD4BS MAbs – CD4BS MAbs bound consistently to most isolates of clade D, but poorly to isolates of other clades with the exception of broadly reactive MAb IgG1b12[Nyambi (2000)]

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716 48–16 Env(dis) gp120(dis) no HIV-1 infection human(IgGκ)
Ab type: CD4BS **References:** [Fevrier (1995)]
- 48–16: Broadly cross-reactive, reacts outside the CD4 binding site and V3 region – competes with sera from 45 seropositive subjects – binding affinity 2–5 x 10–9 M [Fevrier (1995)]

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717 50–61A Env(dis) gp120(dis) L HIV-1 infection human(IgGκ)
Ab type: CD4BS **References:** [Fevrier (1995)]
- 50–61A: Neutralizes lab strains LAI and SF2 – competes with sera from 45 seropositive subjects – binding affinity 2.4 x 10–10 M [Fevrier (1995)]

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718 5145A Env(dis) gp120(dis) L HIV-1 infection human(IgG1)
Ab type: CD4BS **References:** [Pinter (1993a), Warrier (1996), Pincus (1996), Alsmadi & Tilley(1998)]
- 5145A: Potent and broadly cross-reactive neutralization of lab strains [Pinter (1993a)]
- 5145A: Synergistic neutralization of HIV-1 when combined with anti-V2 MAb C108G [Warrier (1996)]
- 5145A: A panel of immunotoxins were generated by linking Env MAbs to ricin A – immunotoxins mediated cell killing, but killing was not directly proportional to binding [Pincus (1996)]
- 5145A: A study of 6 anti-Env MAbs and their ability to bind or direct ADCC against target cells infected with IIIB, MN, SF-2, and RF – bound and directed lysis against all four strains [Alsmadi & Tilley(1998)]

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719 558-D Env(dis) gp120(dis) L HIV-1 infection human( )
Ab type: CD4BS **Donor:** Susan Zolla-Pazner (Zollas01@mcrcr6.med.nyu), NYU Med Center, NY, NY
References: [McKeating (1992c), Nyambi (1998)]
- 558-D: Blocks gp120-CD4 binding – binds a panel of mutants all except for 256 S/Y and 262 N/T, which are probably conformationally disruptive [McKeating (1992c)]
- 558-D: Using a whole virion-ELISA method, 18 human MAbs were tested for their ability to bind to a panel of 9 viruses from clades A, B, D, F, G, and H – CD4BS Abs tended to bind weakly without clade specificity to virions, but bound well to soluble gp120 – 558-D did not bind to any B clade viruses, and weakly bound to clade A, C, and G isolates – 559/64-D, 558-D and 1202-D had similar reactivities [Nyambi (1998)]

720	559/64-D (559 559–64D)	Env(dis)	gp120(dis LAI)	L	HIV-1 infection	human(IgG1κ)

Ab type: CD4BS **Donor:** Susan Zolla-Pazner (Zollas01@mcrcr6.med.nyu), NYU Med Center, NY, NY
References: [Karwowska (1992a), McKeating (1992c), Spear (1993), Stamatatos & Cheng-Mayer(1995), Forthal (1995), Jeffs (1996), Hioe (1997), Nyambi (1998), Gorny (2000), Hioe (2000), Nyambi (2000), Hioe (2001), York (2001)]

- 559/64-D: Conformational – reactive with IIIB gp120 in RIP, but not WB assay [Karwowska (1992a)]
- 559/64-D: Did not mediate deposition of complement component C3 on HIV infected cells [Spear (1993)]
- 559/64-D: Called 559–64D – The binding of conformation-dependent anti-V2, anti-V3, and anti-CD4BS MAbs to monomeric and virion-associated gp120 from HIV-1 isolates with differences in cell tropism was studied – CD4BS loop epitopes are somewhat occluded in the oligomeric gp120 epitopes on the virion surface relative to the gp120 monomer as indicated by an increase in the half-maximal binding values to macrophage-tropic isolates SF162 and SF128a and to T-cell tropic SF2 – binding of anti-CD4BS MAbs to SF2 resulted in a significant amount of dissociation of gp120 from virion surface [Stamatatos & Cheng-Mayer(1995)]
- 559/64-D: Neutralizing activity, no ADCC activity, and no viral enhancing activity [Forthal (1995)]
- 559/64-D: Called 559 – slight, not significant increased binding when V1/V2 or V1/V2 and V3 were deleted from gp120 [Jeffs (1996)]
- 559/64-D: Used in the development of resting cell neutralization assay [Hioe (1997)]
- 559/64-D: Using a whole virion-ELISA method, 18 human MAbs were tested for their ability to bind to a panel of 9 viruses from clades A, B, D, F, G, and H – CD4BS Abs tended to bind weakly without clade specificity to virions, but bound well to soluble gp120 – 559/64-D did not bind to any B clade viruses, and weakly bound clade A, C, and G isolates – 559/64-D, 558-D and 1202-D had similar reactivities [Nyambi (1998)]
- 559/64-D: Binding of a panel of 21 MAbs to soluble oligomeric gp140 was compared to gp41 and gp120 monomers – no MAb was oligomer specific, though anti-V3 and CD4BS MAbs reacted better with the oligomer and V2 and C5 tended to favor the monomer – CD4BS MAbs 559/64-D, 654-D, 729-D, 9CL and 1331E bound with a 5–13 fold preference for the oligomer [Gorny (2000)]
- 559/64-D: Ab responses, because of their capacity to alter antigen uptake and processing, can influence helper T cell responses – anti-CD4 binding site MAbs or serum Ig from HIV+ individuals inihibited proliferative responses of gp120 specific T cells – CD4BS MAbs 654-D, 559/64-D, 588-D, 830-D, 1027–30-D, and 1202–30D strongly diminished proliferation [Hioe (2000)]
- 559/64-D: 26 HIV-1 group M isolates (clades A to H) were tested for binding to 47 MAbs, including 6 CD4BS MAbs – CD4BS MAbs bound consistently to most isolates of clade D, but poorly to isolates of other clades with the exception of broadly reactive MAb IgG1b12[Nyambi (2000)]
- 559/64-D: CD4BS MAbs when complexed with gp120, inhibit proliferation of gp120-specific CD4 T-cells and IFN-γ production – anti-CD4BS MAbs inhibit gp120 presentation by altering the uptake and/or processing of gp120 by the APCs, not by blocking of gp120 attachment to CD4 on the surface of APCs [Hioe (2001)]
- 559/64-D: Abs against the V3 loop (50.1, 58.2, 59.1, 257-D, 268-D, 447-52D), CD4BS (IgG1b12, 559–64D, F105), CD4 induced or CD4i (17b), and to gp41 (2F5, F240) each showed similar binding efficiency to Env derived from related pairs of primary and TCLA lines (primary: 168P and 320SI, and TCLA: 168C and 320SI-C3.3), but the TCLA lines were much more susceptible to neutralization suggesting that the change in TCLA lines that make them more susceptible to NAbs alters some step after binding [York (2001)]

721 588-D (588) Env(dis) gp120(dis) L HIV-1 infection human(IgG1κ)

Ab type: CD4BS **Donor:** Susan Zolla-Pazner (Zollas01@mcrcr6.med.nyu), NYU Med Center, NY, NY
References: [Karwowska (1992a), Buchbinder (1992), Moore & Ho(1993), Jeffs (1996), Nyambi (1998), Hioe (2000), Nyambi (2000)]

- 588-D: Conformational – reactive with IIIB gp120 in RIP, but not WB assay [Karwowska (1992a)]
- 588-D: 4-fold increase in neutralization potency for 588-D when combined 1:1 with human MAb 447-D [Buchbinder (1992)]
- 588-D: Weak neutralization of IIIB – strong inhibition of HIV+ human sera binding to IIIB gp120 [Moore & Ho(1993)]
- 588-D: Called 588 – slight, not significant increased binding when V1/V2 or V1/V2 and V3 were deleted from gp120 [Jeffs (1996)]
- 588-D: Using a whole virion-ELISA method, 18 human MAbs were tested for their ability to bind to a panel of 9 viruses from clades A, B, D, F, G, and H – CD4-BS Abs tended to bind weakly without clade specificity to virions, but bound well to soluble gp120 – 588-D did not bind to any B clade viruses, and weakly bound a clade A, C, and G clade isolate – 559/64-D, 558-D and 1202-D reacted had similar reactivities [Nyambi (1998)]
- 588-D: Ab responses, because of their capacity to alter antigen uptake and processing, can influence helper T cell responses – anti-CD4 binding site MAbs or serum Ig from HIV+ individuals inihibited proliferative responses of gp120 specific T cells – CD4BS MAbs 654-D, 559/64-D, 588-D, 830-D, 1027–30-D, and 1202–30D strongly diminished proliferation [Hioe (2000)]
- 588-D: 26 HIV-1 group M isolates (clades A to H) were tested for binding to 47 MAbs, including 6 CD4BS MAbs – CD4BS MAbs bound consistently to most isolates of clade D, but poorly to isolates of other clades with the exception of broadly reactive MAb IgG1b12[Nyambi (2000)]

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722 654-D (654–30D, 654/30D, 654-D100, 654.30D) Env(dis) gp120(dis LAI) L HIV-1 infection human(IgGκ)

Ab type: CD4BS **Donor:** Susan Zolla-Pazner (Zollas01@mcrcr6.med.nyu), NYU Med Center, NY, NY
References: [Karwowska (1993), Laal (1994), Gorny (1994), Stamatatos & Cheng-Mayer(1995), Li (1997), Stamatatos (1997), Gorny (1997), Gorny (1998), Schonning (1998), Nyambi (1998), Stamatatos & Cheng-Mayer(1998), Hioe (1999), Gorny (2000), Hioe (2000), Hioe (2001), Nyambi (2000), Verrier (2001)]

- 654-D: Dissociation constant gp120 IIIB 0.008 – neutralizes IIIB, acts synergistically with anti-V3 MAb 447-52D – reported to be human(IgG1lambda) [Laal (1994)]
- 654-D: Mild oxidation of carbohydrate moieties inhibits binding [Gorny (1994)]
- 654-D: Called 654–30D – The binding of conformation-dependent anti-V2, anti-V3, and anti-CD4BS MAbs to monomeric and virion-associated gp120 from HIV-1 isolates with differences in cell tropism was studied – CD4BS loop epitopes are somewhat occluded in the oligomeric gp120 epitopes on the virion surface relative to the gp120 monomer as indicated by an increase in the half-maximal binding values to macrophage-tropic isolates SF162 and SF128a and to T-cell tropic SF2 – binding of anti-CD4BS MAbs to SF2 resulted in a significant amount of dissociation of gp120 from virion surface [Stamatatos & Cheng-Mayer(1995)]
- 654-D: Called 654–30D – One of 14 human MAbs tested for ability to neutralize a chimeric SHIV-vpu+, which expressed HIV-1 IIIB env [Li (1997)]

- 654-D: Anti-CD4 BS MAb 654–30D and IgG1b12 have comparable binding affinities, neither mediates gp120-virion dissociation, but IgG1b12 can neutralize SF128A and SF162 and 654-D cannot – 654-D actually enhances infection by both viruses in primary macrophages [Stamatatos (1997)]
- 654-D: Called 654-D100 – 654-D100 and IgG1b12 neutralized viruses HIV-BRU and a mutated virus that lacks the V3 loop glycan equally effectively – in contrast, sera from guinea pigs immunized with BRU gp120 neutralize viruses more effectively that lack the V3 glycan[Schonning (1998)]
- 654-D: Using a whole virion-ELISA method, 18 human MAbs were tested for their ability to bind to a panel of 9 viruses from clades A, B, D, F, G, and H – CD4-BS Abs tended to bind very weakly without clade specificity to virions, but bound well to soluble gp120 – 654-D bound only to JRFL [Nyambi (1998)]
- 654-D: Called 654.30D – deleting the V2 loop of neutralization-resistant HIV-1 isolate SF162 does not abrogate its replication in PBMC or macrophages, but it enhances its neutralization sensitivity to sera from patients with B clade infection up to 170-fold, and also enhances sensitivity to sera from clades A through F – deletion of V2 but not V1 slightly allowed neutralization by CD4BS MAb 654.30D [Stamatatos & Cheng-Mayer(1998)]
- 654-D: The presence of leukocyte function-associated molecule 1 (LFA-1) promotes virus infectivity and hinders neutralization, and anti-LFA-1 MAbs can enhance the neutralizing effect of anti-HIV V3 MAb 447-52D and anti-HIV CD4BS MAb IgG1b12 – non-neutralizing anti-HIV CD4BS MAb 654-D did not become neutralizing in the presence of anti-LFA-1 MAbs [Hioe (1999)]
- 654-D: Binding of a panel of 21 MAbs to soluble oligomeric gp140 was compared to gp41 and gp120 monomers – no MAb was oligomer specific, though anti-V3 and CD4BS MAbs reacted better with the oligomer and V2 and C5 tended to favor the monomer – CD4BS MAbs 559/64-D, 654-D, 729-D, 9CL and 1331E bound with a 5–13 fold preference for the oligomer [Gorny (2000)]
- 654-D: Ab responses, because of their capacity to alter antigen uptake and processing, can influence helper T cell responses – CD4BS MAbs or serum Ig from HIV+ individuals inhibited proliferative responses of gp120 specific T cells – MAb 654-D strongly diminished proliferation – there is a discrepancy in isotyping this antibody, previous reports indicated IgG1kappa, while Hioe suggests it is IgG1lambda [Hioe (2000)]
- 654-D: 26 HIV-1 group M isolates (clades A to H) were tested for binding to 47 MAbs, including 6 CD4BS MAbs – CD4BS MAbs bound consistently to most isolates of clade D, but poorly to isolates of other clades with the exception of broadly reactive MAb IgG1b12 – 654-D had the weakest binding among CD4BS MAbs, binding to only 4/26 isolates [Nyambi (2000)]
- 654-D: CD4BS MAbs when complexed with gp120, inhibit proliferation of gp120-specific CD4 T-cells and IFN-γ production – anti-CD4BS MAbs inhibit gp120 presentation by altering the uptake and/or processing of gp120 by the APCs, not by blocking of gp120 attachment to CD4 on the surface of APCs [Hioe (2001)]
- 654-D: A panel of 12 MAbs was used to identify those that could neutralize the dual-tropic primary isolate HIV-1 89.6 – six gave significant neutralization at 2 to 10 μg/ml: 2F5, 50–69, IgG1b12, 447-52D, 2G12, and 670-D – six did not have neutralizing activity: 654-D, 4.8D, 450-D, 246-D, 98–6, and 1281 – no synergy, only additive effects were seen for pairwise combinations of MAbs, and antagonism was noted between gp41 MAbs 50–69 and 98–6, as well as 98–6 and 2F5 [Verrier (2001)]

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723 729-D (729–30D) | Env(dis) | gp120(dis LAI) | L | HIV-1 infection | human(IgG1κ)

Ab type: CD4BS **Donor:** Susan Zolla-Pazner (Zollas01@mcrcr6.med.nyu), NYU Med Center, NY, NY
References: [Laal (1994), D'Souza (1997), Li (1997), Parren (1997b), Gorny (2000)]

- 729-D: Dissociation constant gp120 IIIB 0.025 – neutralizes IIIB, acts synergistically with anti-V3 MAb 447-52D [Laal (1994)]
- 729-D: In a multilaboratory blinded study, failed to consistently neutralize any of nine B clade primary isolates – reported here to have a lambda light chain, but originally reported in [Laal (1994)] to be IgG1kappa [D'Souza (1997)]
- 729-D: Called 720–30D – one of 14 human MAbs tested for ability to neutralize chimeric SHIV-vpu+, which expressed HIV-1 IIIB env [Li (1997)]
- 729-D: Neutralizes TCLA strains, but not primary isolates [Parren (1997b)]
- 729-D: Binding of a panel of 21 MAbs to soluble oligomeric gp140 was compared to gp41 and gp120 monomers – no MAb was oligomer specific, though anti-V3 and CD4BS MAbs reacted better with the oligomer and V2 and C5 tended to favor the monomer – CD4BS MAbs 559/64-D, 654-D, 729-D, 9CL and 1331E bound with a 5–13 fold preference for the oligomer [Gorny (2000)]

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724 830D (830-D) Env(dis) gp120(dis) L human(IgG1κ)

Ab type: CD4BS **References:** [Wyatt (1998), Hioe (2000)]

- 830D: Summary of the implications of the crystal structure of the core of gp120 bound to CD4 and 17b with what is known about mutations that reduce NAb binding – probable mechanism of neutralization by CD4BS Ab is direct interference with CD4 binding [Wyatt (1998)]
- 830D: Ab responses, because of their capacity to alter antigen uptake and processing, can influence helper T cell responses – anti-CD4 binding site MAbs or serum Ig from HIV+ individuals inihibited proliferative responses of gp120 specific T cells – CD4BS MAbs 654-D, 559/64-D, 588-D, 830-D, 1027–30-D, and 1202–30D strongly diminished proliferation [Hioe (2000)]

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725 9CL Env(dis) gp120(dis LAI) HIV-1 infection human( )

Ab type: CD4BS **Donor:** Susan Zolla-Pazner (Zollas01@mcrcr6.med.nyu), NYU Med Center, NY, NY

References: [Gorny (2000)]

- 9CL: Binding of a panel of 21 MAbs to soluble oligomeric gp140 was compared to gp41 and gp120 monomers – no MAb was oligomer specific, though anti-V3 and CD4BS MAbs reacted better with the oligomer and V2 and C5 tended to favor the monomer – CD4BS MAbs 559/64-D, 654-D, 729-D, 9CL and 1331E bound with a 5–13 fold preference for the oligomer [Gorny (2000)]

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726 anti-CD4BS summary Env(dis) gp120(dis) ( )

Ab type: CD4BS **References:** [Thali (1993), Moore & Sodroski(1996)]

- Shared components of MAb epitopes and the discontinuous CD4 binding regions included Thr 257, Asp 368, Glu 370, Lys 421 through Trp 427 and Asp 457 [Thali (1993)]
- Anti-CD4 binding site antibodies (CD4BS) competitively inhibit CD4 binding to monomeric gp120, and they differ in precise dependence on gp120 residues, but generally require Asp-368 and Glu-370 [Moore & Sodroski(1996)]

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727 b11 Env(dis) gp120(dis) human( )
Ab type: CD4BS **References:** [Parren (1998a)]
- b11: The rank order of Fab binding affinity to monomeric gp120 (Loop 2 > 3B3 > b12 = DO8i > b11 > b3 > b14 > b13 > DO142–10 > DA48 > L17) was markedly different than Fab binding affinity to the mature oligomeric form (3B3 > b12 > DO142–10 > Loop 2 > b11 > L17 > b6 > DO8i > b14 > DA48 > b3 > b13) and binding to oligomeric form and neutralization were correlated for both Fabs and MAbs – authors suggest that neutralization is determined by the fraction of Ab sites occupied on a virion irrespective of the epitope [Parren (1998a)]

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728 b13 Env(dis) gp120(dis) human( )
Ab type: CD4BS **References:** [Parren (1995), Parren (1998a)]
- b13: Fab b13 was used as a control in a hu-PBL SCID mouse study – animals were protected from HIV-1 SF2 infection by IgG1b12, somewhat by Fab b12, but not by b13 [Parren (1995), Parren & Burton(1997)]
- b13: The rank order of Fab binding affinity to monomeric gp120 (Loop 2 > 3B3 > b12 = DO8i > b11 > b3 > b14 > b13 > DO142–10 > DA48 > L17) was markedly different than Fab binding affinity to the mature oligomeric form (3B3 > b12 > DO142–10 > Loop 2 > b11 > L17 > b6 > DO8i > b14 > DA48 > b3 > b13) and binding to oligomeric form and neutralization were correlated for both Fabs and MAbs – authors suggest that neutralization is determined by the fraction of Ab sites occupied on a virion irrespective of the epitope [Parren (1998a)]

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729 b14 Env(dis) gp120(dis) human( )
Ab type: CD4BS **References:** [Parren (1998a)]
- b14: The rank order of Fab binding affinity to monomeric gp120 (Loop 2 > 3B3 > b12 = DO8i > b11 > b3 > b14 > b13 > DO142–10 > DA48 > L17) was markedly different than Fab binding affinity to the mature oligomeric form (3B3 > b12 > DO142–10 > Loop 2 > b11 > L17 > b6 > DO8i > b14 > DA48 > b3 > b13) and binding to oligomeric form and neutralization were correlated for both Fabs and MAbs – authors suggest that neutralization is determined by the fraction of Ab sites occupied on a virion irrespective of the epitope [Parren (1998a)]

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730 b3 Env(dis) gp120(dis) human( )
Ab type: CD4BS **References:** [Parren (1997b), Parren (1998a)]
- b3: Neutralizes TCLA strains, but not primary isolates [Parren (1997b)]
- b3: The rank order of Fab binding affinity to monomeric gp120 (Loop 2 > 3B3 > b12 = DO8i > b11 > b3 > b14 > b13 > DO142–10 > DA48 > L17) was markedly different than Fab binding affinity to the mature oligomeric form (3B3 > b12 > DO142–10 > Loop 2 > b11 > L17 > b6 > DO8i > b14 > DA48 > b3 > b13) and binding to oligomeric form and neutralization were correlated for both Fabs and MAbs – authors suggest that neutralization is determined by the fraction of Ab sites occupied on a virion irrespective of the epitope [Parren (1998a)]

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731 b6 Env(dis) gp120(dis) L human( )
Ab type: CD4BS **References:** [Parren (1997b), Parren (1998a)]
- b6: Neutralizes TCLA strains, but not primary isolates [Parren (1997b)]

- b6: The rank order of Fab binding affinity to monomeric gp120 (Loop 2 > 3B3 > b12 = DO8i > b11 > b3 > b14 > b13 > DO142–10 > DA48 > L17) was markedly different than Fab binding affinity to the mature oligomeric form (3B3 > b12 > DO142–10 > Loop 2 > b11 > L17 > b6 > DO8i > b14 > DA48 > b3 > b13) and binding to oligomeric form and neutralization were correlated for both Fabs and MAbs – authors suggest that neutralization is determined by the fraction of Ab sites occupied on a virion irrespective of the epitope [Parren (1998a)]

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732 BM12 Env(dis) gp120(dis) L HIV-1 infection human( )

Ab type: CD4BS **References:** [Kessler 2nd (1995)]

- BM12: Broad cross-clade neutralization of primary isolates – additive effect in combination with MAb 2F5 [Kessler 2nd (1995)]

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733 D20 Env(dis) gp120(dis IIIB) no Vaccine murine(IgG)

Vaccine: *Vector/type:* vaccinia *Strain:* IIIB *HIV component:* oligomeric gp140

Ab type: CD4BS **Donor:** P. Earl, National Institute of Allergy and Infectious Diseases, NIH, Bethesda, MD
References: [Earl (1994), Broder (1994), Richardson (1996), Otteken (1996), Earl (1997), Sugiura (1999)]

- D20: Binding completely blocked by pooled human sera [Broder (1994)]
- D20: Human sera blocked binding in oligomeric ELISA assay to a similar extent for gp41 MAbs D20, D43, D61, and T4 [Richardson (1996)]
- D20: Pulse label experiments of 4 MAbs (D20, D27, T20, and T22) binding to noncleavable gp160 revealed that these anti-CD4 MAbs bound with a delay, and that the epitope formed with a $t_{1/2}$ of about 10 minutes [Otteken (1996)]
- D20: Used for comparison in a study of gp41 antibodies – D20 binds to a greater extent to cell surface expressed Env than any of 38 conformation dependent anti-gp41 MAbs [Earl (1997)]
- D20: A comparison of 25 gp120 specific, conformation dependent MAbs was done – D20 is part of a group of MAbs labeled A1 – all A1 MAbs were broadly cross-reactive with gp160 from B-clade R5, X4, and R5X4 viruses, blocked CD4 binding, were sensitive to mutations in gp120 positions 368 and 370 that directly contact CD4 [Sugiura (1999)]

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734 D21 Env(dis) gp120(dis IIIB) Vaccine murine(IgG)

Vaccine: *Vector/type:* vaccinia *Strain:* IIIB *HIV component:* oligomeric gp140

Ab type: CD4BS **Donor:** P. Earl, National Institute of Allergy and Infectious Diseases, NIH, Bethesda, MD
References: [Earl (1994), Sugiura (1999)]

- D21: A comparison of 25 gp120 specific, conformation dependent MAbs was done – D21 is part of a group of MAbs labeled A1 – all A1 MAbs were broadly cross-reactive with gp160 from B-clade R5, X4, and R5X4 viruses, blocked CD4 binding, were sensitive to mutations in gp120 positions 368 and 370 that directly contact CD4 [Sugiura (1999)]

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735 D24 Env(dis) gp120(dis IIIB) no Vaccine murine(IgG)

Vaccine: *Vector/type:* vaccinia *Strain:* IIIB *HIV component:* oligomeric gp140

Ab type: CD4BS **Donor:** P. Earl, National Institute of Allergy and Infectious Diseases, NIH, Bethesda, MD
References: [Earl (1994), Sugiura (1999)]

- D24: A comparison of 25 gp120 specific, conformation dependent MAbs was done – D24 is part of a group of MAbs labeled B-I, that had limited cross-reactivity – of seven clade B isolates BH8 and B-al were they only two that consistently reacted with B-I MAbs – B-I MAbs fully blocked CD4 binding [Sugiura (1999)]

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736 D25 Env(dis) gp120(dis IIIB) Vaccine murine(IgG)

Vaccine: *Vector/type:* vaccinia *Strain:* IIIB *HIV component:* oligomeric gp140

Ab type: CD4BS **Donor:** P. Earl, National Institute of Allergy and Infectious Diseases, NIH, Bethesda, MD
References: [Earl (1994), Sugiura (1999)]

- D25: A comparison of 25 gp120 specific, conformation dependent MAbs was done – D25 is part of a group of MAbs labeled A1 – all A1 MAbs were broadly cross-reactive with gp160 from B-clade R5, X4, and R5X4 viruses, blocked CD4 binding, were sensitive to mutations in gp120 positions 368 and 370 that directly contact CD4 [Sugiura (1999)]

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737 D28 Env(dis) gp120(dis IIIB) no Vaccine murine(IgG)

Vaccine: *Vector/type:* vaccinia *Strain:* IIIB *HIV component:* oligomeric gp140

Ab type: CD4BS **Donor:** P. Earl, National Institute of Allergy and Infectious Diseases, NIH, Bethesda, MD
References: [Earl (1994), Sugiura (1999)]

- D28: A comparison of 25 gp120 specific, conformation dependent MAbs was done – D28 is part of a group of MAbs labeled B-I, that had limited cross-reactivity – of seven clade B isolates BH8 and B-al were they only two that consistently reacted with B-I MAbs – B-I MAbs fully blocked CD4 binding [Sugiura (1999)]

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738 D35 Env(dis) gp120(dis IIIB) Vaccine murine(IgG)

Vaccine: *Vector/type:* vaccinia *Strain:* IIIB *HIV component:* oligomeric gp140

Ab type: CD4BS **Donor:** P. Earl, National Institute of Allergy and Infectious Diseases, NIH, Bethesda, MD
References: [Earl (1994), Sugiura (1999)]

- D35: A comparison of 25 gp120 specific, conformation dependent MAbs was done – D35 is part of a group of MAbs labeled B-I, that had limited cross-reactivity – of seven clade B isolates BH8 and B-al were they only two that consistently reacted with B-I MAbs – B-I MAbs fully blocked CD4 binding [Sugiura (1999)]

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739 D39 Env(dis) gp120(dis IIIB) Vaccine murine(IgG)

Vaccine: *Vector/type:* vaccinia *Strain:* IIIB *HIV component:* oligomeric gp140

Ab type: CD4BS **Donor:** P. Earl, National Institute of Allergy and Infectious Diseases, NIH, Bethesda, MD
References: [Earl (1994), Sugiura (1999)]

- D39: A comparison of 25 gp120 specific, conformation dependent MAbs was done – D39 is part of a group of MAbs labeled A1 – all A1 MAbs were broadly cross-reactive with gp160 from B-clade R5, X4, and R5X4 viruses, blocked CD4 binding, were sensitive to mutations in gp120 positions 368 and 370 that directly contact CD4 [Sugiura (1999)]

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740 D42 Env(dis) gp120(dis IIIB) Vaccine murine(IgG)

Vaccine: *Vector/type:* vaccinia *Strain:* IIIB *HIV component:* oligomeric gp140

Ab type: CD4BS **Donor:** P. Earl, National Institute of Allergy and Infectious Diseases, NIH, Bethesda, MD
References: [Earl (1994), Sugiura (1999)]

- D42: A comparison of 25 gp120 specific, conformation dependent MAbs was done – D42 is part of a group of MAbs labeled B-I, that had limited cross-reactivity – of seven clade B isolates BH8 and B-al were they only two that consistently reacted with B-I MAbs – B-I MAbs fully blocked CD4 binding [Sugiura (1999)]

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741 D52 Env(dis) gp120(dis IIIB) Vaccine murine(IgG)

Vaccine: *Vector/type:* vaccinia *Strain:* IIIB *HIV component:* oligomeric gp140

Ab type: CD4BS **Donor:** P. Earl, National Institute of Allergy and Infectious Diseases, NIH, Bethesda, MD
References: [Earl (1994), Sugiura (1999)]

- D52: A comparison of 25 gp120 specific, conformation dependent MAbs was done – D52 is part of a group of MAbs labeled B-I, that had limited cross-reactivity – of seven clade B isolates BH8 and B-al were they only two that consistently reacted with B-I MAbs – B-I MAbs fully blocked CD4 binding [Sugiura (1999)]

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742 D53 Env(dis) gp120(dis IIIB) Vaccine murine(IgG)

Vaccine: *Vector/type:* vaccinia *Strain:* IIIB *HIV component:* oligomeric gp140

Ab type: CD4BS **Donor:** P. Earl, National Institute of Allergy and Infectious Diseases, NIH, Bethesda, MD
References: [Earl (1994), Sugiura (1999)]

- D53: A comparison of 25 gp120 specific, conformation dependent MAbs was done – D53 is part of a group of MAbs labeled B-I, that had limited cross-reactivity – of seven clade B isolates BH8 and B-al were they only two that consistently reacted with B-I MAbs – B-I MAbs fully blocked CD4 binding [Sugiura (1999)]

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743 D60 Env(dis) gp120(dis IIIB) no Vaccine murine(IgG)

Vaccine: *Vector/type:* vaccinia *Strain:* IIIB *HIV component:* oligomeric gp140

Ab type: CD4BS **Donor:** P. Earl, National Institute of Allergy and Infectious Diseases, NIH, Bethesda, MD
References: [Earl (1994), Richardson (1996), Sugiura (1999)]

- D60: A comparison of 25 gp120 specific, conformation dependent MAbs was done – D60 is part of a group of MAbs labeled B-I, that had limited cross-reactivity – of seven clade B isolates BH8 and B-al were they only two that consistently reacted with B-I MAbs – B-I MAbs fully blocked CD4 binding [Sugiura (1999)]

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744 DA48 Env(dis) gp120(dis BRU) HIV-1 infection human( )

Ab type: CD4BS **References:** [Parren (1998a), Sullivan (1998a)]

- DA48: The rank order of Fab binding affinity to monomeric gp120 (Loop 2 > 3B3 > b12 = DO8i > b11 > b3 > b14 > b13 > DO142–10 > DA48 > L17) was markedly different than Fab binding affinity to the mature oligomeric form (3B3 > b12 > DO142–10 > Loop 2 > b11 > L17 > b6 > DO8i > b14 > DA48 > b3 > b13) and binding to oligomeric form and neutralization were correlated for both Fabs and MAbs – authors suggest that neutralization is determined by the fraction of Ab sites occupied on a virion irrespective of the epitope [Parren (1998a)]

- DA48: The HIV-1 virus YU2 entry can be enhanced by MAbs binding to the CD4BS, V3 loop, and CD4i epitopes – the activation for this enhanced entry state could be conferred on HxB2 by introducing the YU2 V3 loop, or the YU2 V3 and V1/V2 loops – a similar effect is observed by sub-neutralizing concentrations of sCD4 and the effect is dependent of CCR5 – Fab Ab fragment DA48 also enhances YU2 entry, ruling out Fc interactions or Env cross-linking as a mechanism – while DA48 enhances YU2, it neutralizes HXBc2 – DA48 was obtained by panning libraries derived from bone marrow from a >15 year long term non-progressor against BRU gp120 [Sullivan (1998a)]

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745 DO8i | Env(dis) | gp120(dis BRU) | | HIV-1 infection | human Fab( )

Ab type: CD4BS **References:** [Parren (1998a)]

- DO8i: The rank order of Fab binding affinity to monomeric gp120 (Loop 2 > 3B3 > b12 = DO8i > b11 > b3 > b14 > b13 > DO142–10 > DA48 > L17) was markedly different than Fab binding affinity to the mature oligomeric form (3B3 > b12 > DO142–10 > Loop 2 > b11 > L17 > b6 > DO8i > b14 > DA48 > b3 > b13) and binding to oligomeric form and neutralization were correlated for both Fabs and MAbs – authors suggest that neutralization is determined by the fraction of Ab sites occupied on a virion irrespective of the epitope [Parren (1998a)]
- DO8i – the HIV-1 virus YU2 entry can be enhanced by MAbs binding to the CD4BS, V3 loop, and CD4i epitopes – the activation for this enhanced entry state could be conferred on HxB2 by introducing the YU2 V3 loop, or the YU2 V3 and V1/V2 loops – a similar effect is observed by sub-neutralizing concentrations of sCD4 and the effect is dependent of CCR5 – Fab fragment DO8i also enhances YU2 entry, ruling out Fc interactions or Env cross-linking as a mechanism, while neutralizing HXBc2 – DO8i was obtained by panning libraries derived from bone marrow from a long term asymptomatic donor against BRU gp120 [Sullivan (1998a)]

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746 F105 (F-105) | Env(dis) | gp120(dis) | L | HIV-1 infection | human(IgG1κ)

Ab type: CD4BS **Donor:** Marshall Posner, Boston MA

References: [Posner (1991), Thali (1991), Thali (1992a), Marasco (1992), Wyatt (1992), Posner (1992b), Posner (1992a), Moore & Ho(1993), Posner (1993), Cavacini (1993a), Cavacini (1993b), Wyatt (1993), Montefiori (1993), Potts (1993), Klasse (1993a), Pincus (1993), Watkins (1993), Bagley (1994), Thali (1994), Cook (1994), Cavacini (1994b), Cavacini (1994a), Earl (1994), Chen (1994a), Turbica (1995), Posner (1995), Cavacini (1995), Sullivan (1995), Khouri (1995), Jagodzinski (1996), Wolfe (1996), McDougal (1996), Wisnewski (1996), Pincus (1996), Litwin (1996), Chen (1996), Parren (1997b), D'Souza (1997), Li (1997), Cao (1997), Wyatt (1997), Wyatt (1998), Cavacini (1998b), Li (1998), Cavacini (1998a), Brand (1998), Sullivan (1998a), Kropelin (1998), Sugiura (1999), Giraud (1999), Cavacini (1999), Oscherwitz (1999), Baba (2000), Park (2000), Kolchinsky (2001), York (2001)]

- F105: First description of F105, binds topographically near the CD4-binding site – inhibits binding of free, infectious virions to uninfected HT-H9 cells, but does not react with virus adsorbed to uninfected HT-H9 cells – soluble rCD4 pre-bound to infected cells inhibits F105 binding – F105 inhibits infection of HT-H9 cells in standard neutralization assays with HIV-1 and MN strains [Posner (1991)]
- F105: F105 neutralization escape mutants result from changes in amino acids in discontinuous regions: C2, 256–262 and C3, 386–370
- F105: Amino acid substitutions that impair F105 neutralization inhibit gp120-CD4 interaction [Thali (1992a)]
- F105: MAb cDNA sequence – V H4 V71–4 rearranged with a D H D-D fusion product of dlr4 and da4, and with J H5 – V κ is from the Humvk325 germline gene joined with Jkappa 2 [Marasco (1992)]

- F105: Precipitation of Δ 297–329 env glycoprotein, which has a deleted V3 loop, is much more efficient than precipitation of wild type [Wyatt (1992)]
- F105: F105 mediates ADCC against SF2 through the CD16+ population of PBMC – does not mediate complement-dependent cytotoxicity [Posner (1992b)]
- F105: Significant enhancement of F105 binding to RF infected cells preincubated with V3-specific MAbs V3–2 and V3–1 [Posner (1992a)]
- F105: Called F-105 – neutralizes IIIB – strong inhibition of HIV+ human sera binding to IIIB gp120 [Moore & Ho(1993)]
- F105: F105 binds to and neutralizes selected lab strains and 3/9 HIV-1 primary isolates – synergistic enhancement of neutralization by seropositive sera [Posner (1993)]
- F105: No neutralization of primary isolates observed (John Moore, pers comm)
- F105: Additive MN or SF2 neutralization when combined with anti-V3 MAbs 447-52D and 257-D [Cavacini (1993a)]
- F105: Serum from all asymptomatic HIV-1 positive people tested block F105 binding, but only from 27% of symptomatic individuals [Cavacini (1993b)]
- F105: Binding to Δ V1/2 and Δ V1/2/3 mutant glycoproteins is 2.4- and 13-fold greater, respectively, than binding to wildtype gp120 [Wyatt (1993)]
- F105: Study of synergism between F105 and sera from vaccinated volunteers with V3-loop specific neutralization activity – 2/3 sera demonstrated neutralization synergy, and 3/3 binding/fusion-inhibition synergy [Montefiori (1993)]
- F105: Study of synergism of neutralization and binding comparing F105 and sCD4 with the V3 MAbs: 50.1, 59.1, 83.1, and 58.2 – synergy was observed, and the data suggest that binding of one ligand (F105) can increase the binding of the second (*e.g.* V3 loop MAbs) due to conformational changes [Potts (1993)]
- F105: The gp41 mutation 582(Ala to Thr) results in conformational changes in gp120 that confer neutralization resistance to a class of conformation sensitive neutralizing MAbs – required >81 fold higher concentrations to neutralize the mutant than wild type [Klasse (1993a)]
- F105: Ab response in IIIB lab workers was compared to gp160 LAI vaccine recipients – F105 was used as a control – infected lab workers and some of the gp160 vaccinees had a MAb response that could inhibit gp120-CD4 binding, at lower titers than the infected lab workers [Pincus (1993)]
- F105: A neutralization escape mutant (HXB2 A281V) was selected by growth of HXB2 in the presence of broadly neutralizing sera – F105 neutralization was not affected by this mutation [Watkins (1993)]
- F105: Comparison of MAb F105 sequences with those of MAbs 21h and 15e [Bagley (1994)]
- F105: A mutation in gp41, 582 A/T, confers resistance to neutralization (also confers resistance to MABs 48d, 21h, 15e and 17b) [Thali (1994)]
- F105: MAbs against the glycosphingolipid GalCer block HIV infection of normally susceptible CD4 negative cells from the brain and colon – anti-CD4 MAbs moderately inhibit gp120 binding to GalCer, possibly through steric hindrance – binding of GalCer to gp120 inhibited but did not completely block F105 binding[Cook (1994)]
- F105: Administered intravenously to four cynomologus monkeys, plasma pharmacokinetics and biological activity tested [Cavacini (1994b)]
- F105: Fab fragments show reduced capacity to neutralize IIIB, MN, and RF compared to intact IgG1, suggesting bivalent interaction may be important in binding and neutralization [Cavacini (1994a)]

- F105: Used as a positive control for CD4 BS antibodies in a study of the influence of oligomeric structure of Env in determining the repertoire of the Ab response [Earl (1994)]
- F105: A human CD4+ T lymphocyte line was transduced to express Fab fragments of F105 – heavy and light chains are joined by an inter-chain linker – in the transduced cells infected with HIV-1, the Fab binds intracellularly to the envelope protein and inhibits HIV-1 production – secreted Fab fragments neutralize cell-free HIV-1 – combined intra- and extracellular binding activities of the expressed Fab make transduced cells resistant to HIV-1 infection and also can protect surrounding lymphocytes by secreting neutralizing antibodies [Marasco1993, Chen (1994a)]
- F105: An immunoassay for titrating CD4BS serum antibody was developed using a gp120-coated solid phase and competition with MAb F105 – 109/110 French HIV-1+ sera and 51/56 HIV-1+ African sera had detectable CD4BS Abs using this assay, demonstrating CD4 binding site conservation among diverse subtypes – CD4BS Abs were detected soon after seroconversion and persisted – 0/21 HIV-2+ sera reacted, indicating that the HIV-1 and HIV-2 CD4BS Abs are not cross-reactive [Turbica (1995)]
- F105: Eight patient phase Ia trial for use as an immunotherapeutic – no clinical or biochemical side effects observed, plasma levels of 10 μg/ml maintained for 21 days [Posner (1995)]
- F105: Efficient neutralization of T-cell adapted lines HXBc2 and MN, no neutralization of primary isolates 89.6, ADA and YU2 – even some enhancement of infection of ADA and YU2 was observed [Sullivan (1995)]
- F105: Biotinylated F105 was used for competition studies with Ab derived from pregnant HIV-1+ women – a correlation between maternal anti-CD4 BS Abs overlapping the F105 binding site and lack of HIV-1 transmission to infants was noted [Khouri (1995)]
- F105: Changing heavy chain from IgG1 to IgG3 increased neutralization efficiency [Cavacini (1995)]
- F105: The sulfated polysaccharide curdlan sulfate (CRDS) binds to the Envelope of T-tropic viruses and neutralizes virus – deletion of the V3 loop results in less potent inhibition of F105 binding by CRDS – binding site of F105 described as 256–257 ST, 368–370 DPE, 421 K, and 470–484 PGGGDMRDNWRSELY [Jagodzinski (1996)]
- F105: Phase I study – MAb clearance in plasma has a 13 day half-life [Wolfe (1996)]
- F105: Neutralizes HIV-1 LAI less potently than V3 specific MAbs [McDougal (1996)]
- F105: F105 is V H4 – V-region heavy chain usage was examined and a bias of enhanced V H1 and V H4, and reduced V H3, was noted among HIV infected individuals [Wisnewski (1996)]
- F105: A panel of immunotoxins were generated by linking Env MAbs to ricin A – immunotoxins mediated cell killing, but killing was not directly proportional to binding [Pincus (1996)]
- F105: Binding of F105 to oligomeric gp120 occurs despite the fact it cannot neutralize primary isolates [Litwin (1996)]
- F105: Intracellular co-expression of heavy and light chains of the Fab105 fragment MAb F105 was enhanced by inclusion of an internal ribosome entry site (IRES) sequence – the Fab105 IRES expression cassette was cloned into an adeno-associated virus (AAV) shuttle vector, and transduced into human lymphocytes which were able to produce and secrete the Fab105 fragments while maintaining normal growth – several primary HIV-1 patient isolates were effectively blocked [Chen (1996)]
- F105: Neutralizes TCLA strains, but not primary isolates [Parren (1997b)]
- F105: In a multilaboratory blinded study, failed to neutralize any of nine B clade primary isolates [D'Souza (1997)]
- F105: One of 14 human MAbs tested for ability to neutralize a chimeric SHIV-vpu+, which expressed HIV-1 IIIB env – F105 could only achieve 50% neutralization alone – all Ab combinations tested showed synergistic neutralization – F105 has synergistic response with MAbs 694/98-D (anti-V3), 48d, 2F5, and 2G12, and also with HIVIG [Li (1997)]

- F105: Virus with the V1-V2 loop deleted was viable and more susceptible to neutralization by CD4i MAb 17b, and anti-V3 MAbs 1121, 9284, and 110.4, but not to a CD4BS MAb, F105 or sCD4 [Cao (1997)]
- F105: Binds both gp120 and soluble gp120+gp41 complex efficiently, suggesting its gp120 epitope is not blocked by gp41 binding – does not bind to HXBc2 gp120 if the 19 C-term amino acids, in conjunction with C1 positions 31–93, are deleted [Wyatt (1997)]
- F105: Summary of the implications of the crystal structure of the core of gp120 bound to CD4 and 17b with what is known about mutations that reduce NAb binding – probable mechanism of neutralization by CD4BS Ab is direct interference with CD4 binding [Wyatt (1998)]
- F105: Phase I dose escalation study, single dose of 100 or 500 mg/m2 was given to 4 HIV+ patients – sustained levels, no immune response against F105, no toxicity, infused Ab retained function – there was no evidence of anti-HIV-1 activity and virus was not diminished at day 1 or 7, by culture or plasma RNA [Cavacini (1998b)]
- F105: Neutralization synergy was observed when the MAbs 694/98-D (V3), 2F5 (gp41), and 2G12 (gp120 discontinuous) were used in combination, and even greater neutralizing potential was seen with the addition of a fourth MAb, F105 (CD4 BS) [Li (1998)]
- F105: The MAb F240 binds to the immunodominant region of gp41 and enhances infection in the presence of complement – reactivity of F240 is enhanced by preincubation of cells with sCD4 or anti-CD4BS MAb F105 [Cavacini (1998a)]
- F105: Immunoprecipitation of gp120 and gp160 expressed from a rec Semliki Forest virus by F105 and IgG1b12 indicated that the SFV expressed HIV-1 Env was folded appropriately – and SVF-HIV-1 Env vaccine gave the strongest anti-HIV-1 Env response in mice, when compared to an HIV-1 Env DNA vaccine and a rgp160 protein [Brand (1998)]
- F105: A comparison of 25 gp120 specific, conformation dependent MAbs was done and F105 was used for competition studies – F105 did cross-compete with multiple CD4BS specific MAbs, however most could not neutralize even the autologous NL4–3 strains [Sugiura (1999)]
- F105: F105 enhances viral entry of viruses carrying the YU2 envelope glycoproteins, but neutralizes HXBc2 [Sullivan (1998a)]
- F105: Anti-C1 region MAb 87–135/9 blocks gp120 interaction with CD4+ cells – blocking activity is additive when combined with antibodies which bind in the C4 region of gp120 (F105, 388/389, and b12) [Kropelin (1998)]
- F105: A triple combination of 2F5, F105 and 2G12 effectively neutralized perinatal infection of macaque infants when challenged with SHIV-vpu+ – the plasma half-life was 7.2 ± 2.2 days [Baba (2000)]
- F105: Host encoded intercellular adhesion molecule (ICAM-1) is incorporated by the HIV-1 virion and enhances viral infectivity – ICAM-1 does not modify virus sensitivity to antibodies 0.5β or 4.8D or sCD4, but neutralizing ability of F105 was diminished in ICAM bearing virions in the presence of lymphocyte function-association antigen-1 (LFA-1) Ab [Fortin (2000)]
- F105: Six mutations in MN change the virus from a high-infectivity neutralization resistant phenotype to low-infectivity neutralization sensitive – V3, CD4BS, and CD4i MAbs are 20–100 fold more efficient at neutralizing the sensitive form, although F105 was an exception and cannot neutralize either form of MN – the mutation L544P reduced binding of all MAbs against gp120 by causing conformational changes [Park (2000)]
- F105: Mutations in two glcosylation sites in the V2 region of HIV-1 ADA at positions 190 and 197 (187 DNTSYRLINCNTS 199) cause the virus to become CD4-independent and able to enter cells through CCR5 alone – these same mutations tended to increase the neutralization sensitivity of the virus, including to F105 [Kolchinsky (2001)]

- F105: Abs against the V3 loop (50.1, 58.2, 59.1, 257-D, 268-D, 447-52D), CD4BS (IgG1b12, 559–64D, F105), CD4i (17b), and to gp41 (2F5, F240) each showed similar binding efficiency to Env derived from related pairs of primary and TCLA lines (primary: 168P and 320SI, and TCLA: 168C and 320SI-C3.3), but the TCLA lines were much more susceptible to neutralization suggesting that the change in TCLA lines that make them more susceptible to NAbs alters some step after binding [York (2001)]
- F105: NIH AIDS Research and Reference Reagent Program: 857

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747 F91 (F-91) Env(dis) gp120(dis) ( )

Ab type: CD4BS **Donor:** J. Robinson, University of Connecticut, Storrs

References: [Moore & Ho(1993), Moore (1994b), Moore & Sodroski(1996), Fouts (1997), Mondor (1998), Parren (1998a), Binley (1998), Fouts (1998)]

- F91: Called F-91 – neutralizes IIIB – reactive with SF-2 gp120 – strong inhibition of HIV+ human sera binding to IIIB gp120 [Moore & Ho(1993)]
- F91: Has strong cross-reactivity with gp120 monomers from most subtypes, A-F [Moore (1994b)]
- F91: Unusual pattern of reciprocal enhancement with several anti-V2 and V3 directed MAbs – reciprocal inhibition of other CD4BS MAbs [Moore & Sodroski(1996)]
- F91: Study shows neutralization is not predicted by MAb binding to JRFL monomeric gp120, but is associated with oligomeric Env binding – F91 bound monomer, did not bind oligomer or neutralize JRFL [Fouts (1997)]
- F91: Weak inhibition of binding of Hx10 to CD4 positive or negative cells, weakly neutralizing [Mondor (1998)]
- F91: The MAb and Fab binding to the oligomeric form of gp120 and neutralization were highly correlated – authors suggest that neutralization is determined by the fraction of Ab sites occupied on a virion irrespective of the epitope [Parren (1998a)]
- F91: A panel of MAbs were shown to bind with similar or greater affinity and similar competition profiles to a deglycosylated or variable loop deleted core gp120 protein (Δ V1, V2, and V3), thus such a core protein produces a structure closely approximating full length folded monomer – CD4BS MAbs 15e, F91 and IgG1b12 bound better to the deleted protein than to wild type [Binley (1998)]
- F91: CD4BS MAbs 15e, 21h, and F91 bind with even lower affinity than 205-43-1 and 205-42-15 to JRFL oligomer – conclusions of this paper contrast with [Parren (1998a)] [Fouts (1998)]

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748 GP13 Env(dis) gp120(dis) L HIV-1 infection human(IgG1)

Ab type: CD4BS **References:** [Schutten (1993), Back (1993), Bagley (1994), Schutten (1995a), Schutten (1995b), Bolmstedt (1996), Wisnewski (1996), Schutten (1996), Schutten (1997)]

- GP13: Neutralized a broad range of HIV-1 strains from phylogenetically different subfamilies – the following gp120 amino acid substitutions strongly inhibit binding: 256(S/Y), 257(T/G), 262(N/T), 368(D/R or K), 370(E/R or Q or D), 384(Y/E) [Schutten (1993)]
- GP13: Mutations in a neutralization resistant isolate obtained by passage of the IIIB isolate in chimpanzees reduced neutralization, but the escape was not as clear as seen with anti-V3 MAbs [Back (1993)]
- GP13: Neutralizes IIIB – only slight inhibition of SI phenotype, and strong enhancement of NSI phenotype chimeric viruses, that incorporated different envs from the same donor [Schutten (1995a)]
- GP13: Neutralizes T-cell adapted viruses but not the SI strain 16.2, despite high binding affinity [Schutten (1995b)]
- GP13: Sera were obtained from guinea pigs vaccinated either with gp160, or with gp160 lacking N-linked glycans at N406, N448, and N463 – these sera could block equally well both the CD4 BS MAb GP13 and the V3 MAb F58/H3 [Bolmstedt (1996)]

- GP13: GP13 is V H5 – V-region heavy chain usage was examined and a bias of enhanced V H1 and V H4, and reduced V H3, was noted among HIV infected individuals [Wisnewski (1996)]
- GP13: IIIB neutralizing MAbs *in vitro* fail to neutralize in a mouse model *in vivo* [Schutten (1996)]
- GP13: Neutralized (50%) an SI-env chimeric virus and enhanced (>5 fold) an NSI-env chimeric virus [Schutten (1997)]
- GP13: UK Medical Research council AIDS reagent: ARP3054

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749 GP44 Env(dis) gp120(dis) L HIV-1 infection human(IgG1)

Ab type: CD4BS **References:** [Schutten (1993), Bagley (1994), Wisnewski (1996)]

- GP44: Exhibited a more restricted pattern of neutralizing activity than GP13 and GP68 – the following gp120 amino acid substitutions strongly inhibit binding: 256(S/Y), 257(T/G), 262(N/T), 368(D/R or K), 370(E/R or Q or D) [Schutten (1993)]
- GP44: GP44 is V H1 – V-region heavy chain usage was examined and a bias of enhanced V H1 and V H4, and reduced V H3, was noted among HIV infected individuals [Wisnewski (1996)]

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750 GP68 Env(dis) gp120(dis) L HIV-1 infection human(IgG1)

Ab type: CD4BS **References:** [Schutten (1993), Klasse (1993a), Bagley (1994), Schutten (1995a)]

- GP68: Neutralized a broad range of HIV-1 lab strains from phylogenetically different subfamilies – the following gp120 amino acid substitutions strongly inhibit binding: 117(K/W), 256(S/Y), 257(T/G), 262(N/T), 368(D/R or K), 370(E/R or Q), 384(Y/E), 435(Y/H) [Schutten (1993)]
- GP68: The gp41 mutation 582(Ala to Thr) results in conformational changes in gp120 that confer neutralization resistance to a class of conformation sensitive neutralizing MAbs – GP68 required markedly higher concentrations to neutralize the mutant than wild type [Klasse (1993a)]
- GP68: Neutralizes IIIB – only slight inhibition of SI phenotype, and strong enhancement of NSI phenotype chimeric viruses, that incorporated different envs from the same donor [Schutten (1995a)]
- GP68: GP68 is V H1 – V-region heavy chain usage was examined and a bias of enhanced V H1 and V H4, and reduced V H3, was noted among HIV infected individuals [Wisnewski (1996)]
- GP68: UK Medical Research Council AIDS reagent: ARP3055

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751 HF1.7 Env(dis) gp120(dis) L anti-idiotype murine(IgM)

Ab type: CD4BS **References:** [Chanh (1987)]

- HF1.7: An anti-Id antibody stimulated by anti-CD4 MAb Leu-3a binds to recombinant gp160, suggesting HF1.7 mimics CD4 [Chanh (1987)]

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752 HT5 (205-43-1) Env(dis) gp120(dis) L (weak) HIV-1 infection human( )

Ab type: CD4BS **Donor:** Ciba-Geigy AG (Basel, Switzerland), and Tanox Biosystems, Houston, Texas
References: [Moore (1994b), Moore (1995a), Fouts (1997), Fouts (1998)]

- HT5: HT5, HT6, and HT7 are also known as 205-43-1, 205-42-15, and 205-46-9, respectively [Fouts (1998)]
- HT5: Despite highly cross-reactive binding to many primary and T-cell adapted viral strains, only weakly neutralizes IIIB and MN [Moore (1995a)]

- HT5: 205-46-9 was cross-reactive across clades A-F, 205-43-1 very cross-reactive but not quite as extensive 205-46-9 [Moore (1994b)]
- HT5: MAbs IgG1b12, HT5, HT6, and HT7 cross-compete for binding to monomeric gp120, bind equally well, inhibit gp120-sCD4 interactions, but only IgG1b12 neutralizes JRFL [Fouts (1997)]
- HT5: HT5 and HT6 bind JRSF oligomer but with low affinity, and are not neutralizing – conclusions of this paper contrast with [Parren (1998a)] [Fouts (1998)]

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753 HT6 (205-42-15) | Env(dis) | gp120(dis) | L (weak) | HIV-1 infection | human( )

Ab type: CD4BS **Donor:** Ciba-Geigy AG Basel, Switzerland, and Tanox Biosystems, Houston, Texas
References: [Moore (1994b), Moore (1995a), Fouts (1997), Fouts (1998)]

- HT6: HT5, HT6, and HT7 are also known as 205-43-1 , 205-42-15, and 205-46-9, respectively [Fouts (1998)]
- HT6: Despite highly cross-reactive binding to many primary and T-cell adapted viral strains, only weakly neutralizes IIIB and MN [Moore (1995a)]
- HT6: 205-46-9 was cross-reactive across clades A-F, 205-43-1 was not quite as extensively cross-reactive [Moore (1994b)]
- HT6: MAbs IgG1b12, HT5, HT6, and HT7 cross-compete for binding to monomeric gp120, bind equally well, inhibit gp120-sCD4 interactions, but only IgG1b12 neutralizes JRFL [Fouts (1997)]
- HT6: HT5 and HT6 bind JRSF oligomer but with low affinity, and are not neutralizing – conclusions of this paper contrast with [Parren (1998a)] [Fouts (1998)]

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754 HT7 (205-46-9) | Env(dis) | gp120(dis) | L (IIIB) | HIV-1 infection | human( )

Ab type: CD4BS **Donor:** Ciba-Geigy AG (Basel, Switzerland), and Tanox Biosystems, Houston, Texas
References: [Moore (1994b), Moore (1995a), Fouts (1997), Fouts (1998)]

- HT7: HT5, HT6, and HT7 are also known as 205-43-1 , 205-42-15, and 205-46-9, respectively [Fouts (1998)]
- HT7: Despite highly cross-reactive binding to many primary and T-cell adapted viral strains, only neutralizes IIIB well, with sporadic weak neutralization of other isolates [Moore (1995a)]
- HT7: 205-46-9 was cross-reactive across clades A-F, 205-43-1 was cross-reactive, but not quite as extensive [Moore (1994b)]
- HT7: MAbs IgG1b12, HT5, HT6, and HT7 cross-compete for binding to monomeric gp120, bind equally well, inhibit gp120-sCD4 interactions, but only IgG1b12 neutralizes JRFL [Fouts (1997)]
- HT7: Binds JRSF oligomer with high affinity, at least as high as IgG1b12, but IgG1b12 is neutralizing, H7 is not – conclusions of this paper contrast with [Parren (1998a)] – authors propose a model where H7 may inhibit CD4 binding, but cause a conformational shift which enhances CCR5 binding and thus counteracts the neutralizing effect [Fouts (1998)]

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755 ICR 39.13g (ICR39.13g, 39.13g) | Env(dis) | gp120(dis) | L | Vaccine | rat(IgG2b)

Vaccine: *Vector/type:* recombinant protein *Strain:* BH10 *HIV component:* gp120

Ab type: CD4BS **Donor:** Jackie Cordell and C. Dean

References: [Cordell (1991), McKeating (1992a), McKeating (1992c), McKeating (1993b), Moore & Ho(1993), Thali (1993), Klasse (1993a), McLain & Dimmock(1994), Beretta & Dalgleish(1994), McKeating (1996), Armstrong & Dimmock(1996), Klasse & Sattentau(1996), Peet (1998)]

- ICR 39.13g: Cross-competes with MAbs ICR 39.3b and 15e [Cordell (1991)]
- ICR 39.13g: Binds to a conformational epitope involved in CD4 binding – exerts a synergistic effect in combination with V3 directed MAbs [McKeating (1992a)]
- ICR 39.13g: Neutralization activity against HXB10, RF, SF-2 and MN strains of HIV-1 [McKeating (1993b)]
- ICR 39.13g: Conformational, does not bind denatured gp120 – weak neutralization of IIIB – strong inhibition of HIV+ human sera binding to IIIB gp120 [Moore & Ho(1993)]
- ICR 39.13g: Strongly inhibits CD4 inducible MAb 48d [Thali (1993)]
- ICR 39.13g: Kinetics of neutralization studied – no lag for 39.3b, while ICR 39.13g and ICR 41.1i have lags of 5 and 15 min respectively – mediates neutralization with 2.3 molecules of IgG [McLain & Dimmock(1994)]
- ICR 39.13g: The gp41 mutation 582(Ala to Thr) results in conformational changes in gp120 that confer neutralization resistance to a class of conformation sensitive neutralizing MAbs – ICR 39.13g required moderately higher concentrations to neutralize the mutant than wild type [Klasse (1993a)]
- ICR 39.13g: Called 39.13g Neutralizes HXB2, but fails to neutralize chimeric virus with gp120 from primary isolates in an HXB2 background [McKeating (1996)]
- ICR 39.13g: Post-attachment neutralization mechanism, in contrast to MAb 39.3b [Armstrong & Dimmock(1996)]
- ICR 39.13g: Variants of LAI have differing neutralization susceptibility to 39.13g [Klasse & Sattentau(1996)]
- ICR 39.13g: The most variable amino acids in the V3 loop were replaced with serines to make the immunodominant V3 loop less immunogenic – these changes did not affect the ability of sCD4 or MAbs to V1/V2, C1 and C4 to bind – ICR 39.13g was not affected by V3 serine substitutions – mice injected with serine substituted gp120 had a reduced response relative to wildtype, and no enhanced immunogenicity of conserved regions [Peet (1998)]
- ICR 39.13g: UK Medical Research Council AIDS reagent: ARP390

756	ICR 39.3b (39.3, 39.3b, ICR39.3b)	Env(dis)	gp120(dis)	L	Vaccine	rat(IgG2b)

Vaccine: *Vector/type:* recombinant protein *Strain:* BH10 *HIV component:* gp120

Ab type: CD4BS **Donor:** J. Cordell and C. Dean

References: [Cordell (1991), McKeating (1992c), Moore (1993b), McLain & Dimmock(1994), Armstrong & Dimmock(1996), Jeffs (1996), Wyatt (1998)]

- ICR 39.3b: also known as 39.3, 39.3b and ICR39.3b
- ICR 39.3b: Cross-competes with MAbs ICR 39.13g and 15e [Cordell (1991)]
- ICR 39.3b: Conformational, does not bind to denatured IIIB [Moore & Ho(1993)]
- ICR 39.3b: Kinetics of neutralization studied – no lag for 39.3b, while ICR 39.13g and ICR 41.1i have lags of 5 and 15 min respectively [McLain & Dimmock(1994)]

- ICR 39.3b: Neutralizes only if the antibody is added prior to the attachment of the virus to the cell, in contrast to 39.13g [Armstrong & Dimmock(1996)]
- ICR 39.3b: Called 39.3b – increased binding when V1/V2 or V1/V2 and V3 were deleted from gp120 [Jeffs (1996)]
- ICR 39.3b: Called 39.3 – summary of the implications of the crystal structure of the core of gp120 bound to CD4 and 17b with what is known about mutations that reduce NAb binding – probable mechanism of neutralization by CD4BS Ab is direct interference with CD4 binding [Wyatt (1998)]
- ICR 39.3b: UK Medical Research Council AIDS reagent: ARP391

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757 IgG1b12 (Fab b12, Fab 3B3, MAb IgG1b12, IgG1-b12, IgG1 b12, IgGB12, b4/12, b12, 1b12) | Env(dis) | gp120(dis) | L P | HIV-1 infection | human(IgG1κ)

Ab type: CD4BS **Donor:** D. Burton, Scripps Research Institute, La Jolla, CA, also J. Geltowsky and J. Pyati, R. W. Johnson Pharmaceutical Research Inst. La Jolla, CA

References: [Burton (1991), Barbas III (1992), Roben (1994), Burton (1994), Moore (1994b), Sattentau(1995), Moore (1995a), Moore & Ho(1995), Parren (1995), Trkola (1995), Ditzel (1995), Sullivan (1995), Yang (1997), Moore & Sodroski(1996), Gauduin (1996), Poignard (1996b), Poignard (1996a), Trkola (1996a), Sattentau(1996), McKeating(1996), D'Souza (1997), Schutten (1997), Mo (1997), Fouts (1997), Li (1997), Kessler II (1997), Moore & Trkola(1997), Stamatatos (1997), Ditzel (1997), Ugolini (1997), Wyatt (1997), Burton & Montefiori(1997), Boots (1997), Parren (1997b), Parren (1997a), Parren & Burton(1997), Valenzuela (1998), Wyatt (1998), Mondor (1998), Parren (1998a), Connor (1998), Binley (1998), Fouts (1998), Takefman (1998), Parren (1998b), Brand (1998), Schonning (1998), Sullivan (1998a), Frankel (1998), Kropelin (1998), Stamatatos & Cheng-Mayer(1998), Poignard (1999), Jackson (1999), Hioe (1999), Montefiori & Evans(1999), Giraud (1999), Beddows (1999), Binley (1999), Grovit-Ferbas (2000), Ly & Stamatatos(2000), Nyambi (2000), Park (2000), Kolchinsky (2001), Saphire (2001a), Saphire (2001b), Yang (2001), York (2001), Zwick (2001a), Zwick (2001b), Zwick (2001c), Poignard (2001), Zeder-Lutz (2001), Spenlehauer (2001), Verrier (2001), Hofmann-Lehmann (2001), Xu (2001), Srivastava (2002)]

- IgG1b12: Fab b12 was derived from IgG1b12, Fab 3B3 was derived from Fab b12 by random mutagenesis and selected for increased affinity to sgp120
- IgG1b12: The original Fab fragment was derived from a combinatorial phage library from bone marrow of an HIV-1 positive individual who had been asymptomatic for six years [Burton (1991)]
- IgG1b12: Anti-CD4 binding site Fab, potent neutralizing activity, greater affinity for a subpopulation of gp120 molecules suggested to be in a mature confirmation – mutations in gp120 that abrogate binding: 368 D/R or D/T, 370 E/R, and 477 D/V, of clone HXBc2 of LAI – sensitive to V1 and V2 substitutions [Roben (1994)]
- IgG1b12: Very potent neutralization, of primary and lab strains, at concentrations that could be achieved by passive immunization – reduced binding with A,C, and D clade viruses relative to B clade, poor reactivity with E clade – isolates that were refractive to neutralization by sera from HIV-1+ donors could be neutralized by IgG1 b12 [Burton (1994)]
- IgG1b12: Cross-reactive with some gp120s, (but not all), from clades A-D – not reactive with gp120 from clades E or F [Moore (1994b)]
- IgG1b12: Formalin inactivation of virus at 0.1% formalin for 10 hours at 4 degrees was optimal for inactivation of virus while maintaining epitope integrity [Sattentau (1995)]
- IgG1b12: Anti-CD4 binding site MAb – very potent neutralization of a number of primary isolates [Moore (1995a)]

- IgG1b12: Complete protection against HIV-1 infection was achieved in hu-PBL-SCID mice by passive immunization with physiologically relevant doses – pharmacokinetics showed serum half-life of 30.2 $\pm$ 1.3 hours for Fab b12 and 7.4 $\pm$ 0.7 days for IgG1 b12 in mice, but IgG1 half-lives in human are generally between 21–23 days [Parren (1995), Parren & Burton(1997)]
- IgG1b12: Called BM12 – broad cross-clade neutralization of primary isolates – additive neutralization in combination with MAb 2F5 [Kessler 2nd (1995)]
- IgG1b12: Review: unusual properties for anti-CD4 BS MAb: sensitive to V2 substitutions, preferential recognition of the oligomer on the cell surface [Moore & Ho(1995)]
- IgG1b12: Could potently neutralize primary isolates from within clade B, but showed a slight reduction in efficacy outside of clade B [Trkola (1995)]
- IgG1b12: Because Fab b12 shows reduction in binding when the V2 loop is deleted and when aa 183/184 PI/SG substitutions are made competition studies were done with Fab L78 and anti-V2 MAbs SC258 and 684–238 and they do not compete with IgG1b12 [Ditzel (1995)]
- IgG1b12: Fab b12 showed potent neutralization of T-cell-line-adapted strains, but much reduced neutralization of 3 primary isolates – 2 of the 3 primary isolates also had reduced binding affinity, but the third was as efficiently immunoprecipitated as HXBc2 [Sullivan (1995)]
- IgG1b12: Saturation mutagenesis of the complementarity-determining region and optimization strategies were used to create very high affinity versions of this Fab – increased affinity was dominated by a slowing of the off rate [Yang (1997)]
- IgG1b12: Potent neutralizing *ex vivo* of virus taken directly from plasma of HIV-1 infected individuals – little correlation between neutralization sensitivity of passaged virus and plasma derived virus – more effective than MAb 19b [Gauduin (1996)]
- IgG1b12: Review: Unique among anti-CD4BS MAbs in terms of being potent against both lab adapted virus and primary isolates – one of three MAbs (IgG1b12, 2G12, and 2F5) generally accepted as having significant potency against primary isolates [Poignard (1996b)]
- IgG1b12: Anti-CD4BS MAbs 15e, 21h, and IgG1b12 did not cause gp120 dissociation from virus, or exposure of the gp41 epitope of MAb 50–69, in contrast to CD4i MAb 48d and anti-V3 neutralizing MAbs [Poignard (1996a)]
- IgG1b12: Neutralizes JR-FL – inhibits gp120 interaction with CCR-5 in a MIP-1β-CCR-5 competition study [Trkola (1996a)]
- IgG1b12: Review: Only four epitopes have been described which can stimulate a useful neutralizing response to a broad spectrum of primary isolates, represented by the binding sites of MAbs: 447-52-D, 2G12, Fab b12, and 2F5 [Sattentau(1996)]
- IgG1b12: In a multilab evaluation of monoclonal antibodies, only IgG1b12, 2G12, and 2F5 could neutralize at least half of the 9 primary test isolates at a concentration of < 25 μg per ml for 90% viral inhibition – IgG1b12 failed to neutralize only 1/9 primary isolates, although there was some variation between test sites [D'Souza (1997)]
- IgG1b12: Inhibited some SI- and NSI-env chimeric viruses but enhanced one NSI-env chimeric virus 3 fold [Schutten (1997)]
- IgG1b12: JRCSF was cultured in the presence of IgG1b12 until a 100-fold resistance to neutralization was selected – resistance was due to three changes: V2 substitution D182N and C3 substitution P365L conferred resistance, and V2 D164N was also required for a viable virus – IgG1b12 resistant virus remained sensitive to MAbs 2G12 and 2F5 [Mo (1997)]
- IgG1b12: Study shows neutralization is not predicted by MAb binding to JRFL monomeric gp120, but is associated with oligomeric Env binding – IgG1b12 bound monomer, oligomer, and neutralized JRFL [Fouts (1997)]

- IgG1b12: b12 was used in its IgG1 form – of 14 human MAbs, the most potent neutralizer of SHIV-vpu+, which expressed HIV-1 IIIB env – all Ab combinations tested showed synergistic neutralization – b12 has a synergistic response with MAbs 694/98-D (anti-V3), 2F5, and 2G12 [Li (1997)]
- IgG1b12: 35 primary isolates were tested and all were neutralized by IgG1b12 (including 4, UG270, RW92/026, ZB20, and 301727 which been had reported as not neutralized by IgG1b12 [Trkola (1995)]) – IgG1b12 could neutralize even when added after the virus to the culture – selection for 400-fold increased affinity did not enhance neutralization by antibody – IgG1b12 was more potent with greater breadth than MAb 2F5 [Kessler II (1997)]
- IgG1b12: Review: MABs 2F5, 2G12 and IgG1b12 have potential for use in combination with CD4-IgG2 as an immunotherapeutic or immunoprophylactic – homologous MAbs to these are rare in humans and vaccine strategies should consider including constructs that may enhance exposure of these MAbs‘ epitopes [Moore & Trkola(1997)]
- IgG1b12: Viral binding inhibition by IgG1b12 strongly correlated with neutralization (all other neutralizing MAbs tested showed some correlation except 2F5) [Ugolini (1997)]
- IgG1b12: Major deletions in C1 and C5 and deletions of the V1V2 and V3 loops do not diminish binding [Wyatt (1997)]
- IgG1b12: This is a review that includes a description of IgG1b12, noting approximately equivalent affinities for sgp120 and unprocessed gp160, and somewhat enhanced affinity for the native oligomer on TCLA viruses – primary viruses have reduced affinity, but still in the useful range for neutralization – there can be complete protection in hu-PBL-SCID mice with Ab even when administered several hours after viral challenge – competes with sCD4, but unlike other CD4BS antibodies, it is sensitive to mutations in V2 [Burton & Montefiori(1997)]
- IgG1b12: In this review, the technique and potential application of Fab expression and selection in phage display libraries, and subsequent production of IgG molecules is discussed – b12 is exceptionally potent at neutralization and can successfully neutralize most B clade primary isolates, and many isolates from other subtypes as well – 3B3 was derived from b12 by selection for higher affinity using the CDR walking strategy – 3B3 has 8-fold enhancement of binding, a linear correlation was found between neutralization and affinity, and 3B3 can neutralize strains b12 cannot [Parren & Burton(1997)]
- IgG1b12: Abs that recognize discontinuous epitopes can identify mimotopes from a phage peptide display library – IgG1b12 blocks CD4 binding and is the most potent neutralizing Ab – many 15 and 21-mer phage inserts were recognized, but it was not possible to derive a consensus – common features were a W and at least one acidic residue, and one sequence was found multiple times: NWPRWWEEFVDKHSS, and this peptide could compete with gp120 – two short stretches found in the phage peptides might mimic gp120 components of the epitope: positions 382–384, FFY(I), and 423–426 I(FV)I(V)NM [Boots (1997)]
- IgG1b12: Fab b12 is unusual in that it binds to gp140 and monomeric gp120 with similar affinities, and with a higher affinity to the native oligomer – authors propose this antibody may be exceptional because it binds the virus rather than viral debris – IgG1b12 can protect against infection prior to or shortly after challenge of hu-PBL-SCID mice with TCLA strains and primary strains, but the serum concentrations required were higher than for *in vitro* neutralization [Parren (1997b), Parren (1997a)]
- IgG1b12: MAb was slightly more efficient at neutralization than Fab – inhibits viral binding to cells and viral entry – doesn’t affect CD4-independent binding to T-cells [Valenzuela (1998)]

- IgG1b12: Summary of the implications of the crystal structure of the core of gp120 bound to CD4 and 17b with what is known about mutations that reduce NAb binding – probable mechanism of neutralization by CD4BS Ab is direct interference with CD4 binding – IgG1b12 is an unusual CD4BS antibody because it is particularly potent as a neutralizing antibody and it is susceptible to changes in the V1-V2 stem loop structure, and so it may disrupt an interaction between CD4 and conserved amino acids on the V1-V2 stem [Wyatt (1998)]
- IgG1b12: Enhances binding of Hx10 to CD4 positive or negative HeLa cells, inhibits binding to CD4+ T-cell line A3.01 – neutralizes HeLa and A3.01 cell Hx10 infection [Mondor (1998)]
- IgG1b12: IgG1b12, Fab b12 and 3B3 derived from b12 were all included in this study – the rank order of Fab binding affinity to monomeric gp120 (Loop 2 > 3B3 > b12 = DO8i > b11 > b3 > b14 > b13 > DO142–10 > DA48 > L17) was markedly different than Fab binding affinity to the mature oligomeric form (3B3 > b12 > DO142–10 > Loop 2 > b11 > L17 > b6 > DO8i > b14 > DA48 > b3 > b13) and binding to oligomeric form and neutralization were correlated for both Fabs and MAbs – authors suggest that neutralization is determined by the fraction of Ab sites occupied on a virion irrespective of the epitope – binding affinity of divalent IgG1b12 is 17-fold greater than monovalent Fab b12 [Parren (1998a)]
- IgG1b12: Ab from gp120 vaccinated individuals prior to infection, who subsequently became HIV infected, could not achieve 90% neutralization of the primary virus by which the individuals were ultimately infected – these viruses were not particularly refractive to neutralization, as determined by their susceptibility to neutralization by MAbs 2G12, IgG1b12, 2F5 and 447-52D [Connor (1998)]
- IgG1b12: A panel of MAbs were shown to bind with similar or greater affinity and similar competition profiles to a deglycosylated or variable loop deleted core gp120 protein (Δ V1, V2, and V3), thus such a core protein produces a structure closely approximating full length folded monomer – CD4BS MAbs 15e, F91 and IgG1b12 bound better to the deleted protein than to wild type [Binley (1998)]
- IgG1b12: Binds JRSF oligomer with high affinity, as do 205-46-9 and 2G6, but IgG1b12 is neutralizing, the other two are not – conclusions of this paper contrast with Parren98 – authors propose a model where 205-46-9 and 2G6 may inhibit CD4 binding, but cause a conformational shift which enhances CCR5 binding and thus counteracts the neutralizing effect – rank order of CD4BS antibodies oligomer binding is IgG1b12 = 2G6 = 205-46-9 > 205-43-1 = 205-42-15 > 15e = 21h = F91, and the only thing notably distinguishing about neutralizing IgG1b12 is that it depends on residues in V2 [Fouts (1998)]
- IgG1b12: Induces Complement-mediated lysis in MN but not primary isolates – primary isolates are refractive to CML [Takefman (1998)]
- IgG1b12: MAbs 2G12, 2F5 and b12 are broadly neutralizing, as are some human polyconal sera, but this paper describes a set of primary isolates that are resistant to all three MAbs and 2 broadly neutralizing sera – results indicate that resistance levels of pediatric isolates might be higher than adult isolates – resistance in general did not seem to be conferred by a loss of binding affinity for gp120 or gp41, rather by a more global perturbation of oligomeric Envelope [Parren (1998b)]
- IgG1b12: Immunoprecipitation of gp120 and gp160 expressed from a rec Semliki Forest virus by F105 and IgG1b12 indicated that the SFV expressed HIV-1 Env was folded appropriately – and SVF-HIV-1 Env vaccine gave the strongest anti-HIV-1 Env response in mice, when compared to an HIV-1 Env DNA vaccine and a rgp160 protein [Brand (1998)]
- IgG1b12: MABs 654-D100 and IgG1b12 neutralized viruses HIV-BRU and a mutated virus that lacks the V3 loop glycan equally effectively – in contrast, sera from guinea pigs immunized with BRU gp120 neutralize viruses more effectively that lack the V3 glycan[Schonning (1998)]

- IgG1b12: Fab b12 – the HIV-1 virus YU2 entry can be enhanced by MAbs binding to the CD4BS, V3 loop, and CD4i epitopes – the activation for this enhanced entry state could be conferred on HxB2 by introducing the YU2 V3 loop, or the YU2 V3 and V1/V2 loops – a similar effect is observed by sub-neutralizing concentrations of sCD4 and the effect is dependent of CCR5 – Fab fragment b12 also enhances YU2 entry, ruling out Fc interactions or Env cross-linking as a mechanism, while neutralizing HXBc2 [Sullivan (1998a)]
- IgG1b12: anti-C1 region MAb 87–135/9 blocks gp120 interaction with CD4+ cells – blocking activity is additive when combined with antibodies which bind in the C4 region of gp120 (F105, 388/389, and b12) [Kropelin (1998)]
- IgG1b12: Deleting the V2 loop of neutralization-resistant HIV-1 isolate SF162 does not abrogate its replication in PBMC or macrophages, but it enhances its neutralization sensitivity to sera from patients with B clade infection up to 170-fold, and also enhances sensitivity to sera from clades A through F – deletion of V2, but not V1, diminished neutralization by CD4BS MAb IgG1b12, in contrast to 654.30D and IgGCD4 [Stamatatos & Cheng-Mayer(1998)]
- IgG1b12: Infection of dendritic cells cultured from CD14+ blood cells or from cadaveric human skin was blocked by neutraling MAbs IgG1b12, or 2F5 and 2G12 delivered together, but not by control non-neutralizing anti-gp120 MAb 4.8D, indicating that NAbs could interrupt early mucosal transmission events [Frankel (1998)]
- IgG1b12: The presence of leukocyte function-associated molecule 1 (LFA-1) promotes virus infectivity and hinders neutralization, and anti-LFA-1 MAbs can enhance the neutralizing effect of anti-HIV V3 MAb 447-52D and anti-HIV CD4BS MAb IgG1b12 – non-neutralizing anti-HIV CD4BS MAb 654-D did not become neutralizing in the presence of anti-LFA-1 MAbs [Hioe (1999)]
- IgG1b12: rgp120 derived from a R5X4 subtype B virus was used to vaccinate healthy volunteers and the resulting sera were compared with sera from HIV-1 positive subjects and neutralizing MAbs – TCLA strains showed enhanced IgG1b12 neutralization sensitivity relative to PBMC-adapted lines – IgG1b12 was able to bind, with low affinity, to the rgp120 monomer HIV-1 W61D [Beddows (1999)]
- IgG1b12: A meeting summary presented results regarding neutralization – D. Burton and J. Mascola presented results concerning passive immunization and protection of hu-PBL-SCID mice and macaques, respectively, and both found combinations of MAbs that were able to achieve 99% neutralization *in vitro* corresponded to efficacy *in vivo* [Montefiori & Evans(1999)]
- IgG1b12: does not inhibit attachment of virus to cells and was used as a control of a study of neutralization by a MAb F58 based micro antibody [Jackson (1999)]
- IgG1b12: Hu-PBL-SCID mice were infected with HIV-1s JRCSF and SF162 to study the effect of NAbs on an established infection – at day 6 post infection, mice were given 50 mg/kg of b12, an amount that would have been protective if given up to 8 hours post-infection, and 100-fold higher than the amount required for 90% neutralization *in vitro* – no significant differences in the initial rate of decrease in viral load or the plateau levels of viral RNA between the b12 treated and control mice were seen – in most of the Ab treated mice escape mutants were observed with varying patterns of mutations – a combination of b12, 2G12 and 2F5 protected 1/3 mice, and an isolate from one of the other two was resistant to neutralization by all three MAbs [Poignard (1999)]

- IgG1b12: The MAbs with the broadest neutralizing activity, IgG1b12, 2G12 and 2F5, all have high affinity for the native trimer, indicating that they were raised in an immune response to the oligomer on the virion surface rather than dissociated subunits – a disulfide linked gp120-gp41 (SOS gp140) was created to mimic the native conformation of Env and explore its potential as an immunogen – SOS gp140 is recognized by NAbs IgG1b12, 2G12, and CD4-IgG2, and also by anti-V3 MAbs 19b and 83.1 – SOSgp140 is not recognized by C4 region MAbs that neutralize only TCLA strains, G3-42 and G3-519 – nor did it bind C11, 23A, and M90, MAbs that bind to gp120 C1 and C5, where it interacts with gp41 – MAbs that bind CD4 inducible epitopes, 17b and A32 were very strongly induced by CD4 in SOS gp140 – anti-gp41 MAbs that bind in the region that interacts with gp120, 7B2, 2.2B, T4, T15G1 and 4D4, did not bind to SOSgp140, in contrast to 2F5, which binds to the only gp41 epitope that is well exposed in native gp120-gp41 complexes [Binley (1999)]
- IgG1b12: To determine the antigenicity of virus killed by thermal and chemical inactivation, retention of conformation-dependent neutralization epitopes was examined, and exposure of CD4BS epitopes was found to be enhanced (MAbs IgG1b12, 205-46-9, and 205-43-1) – binding to 2G12 and 447-52D epitopes was essentially unaltered – the 17b CD4i epitope was also exposed [Grovit-Ferbas (2000)]
- IgG1b12: SF162 is a neutralization-resistant HIV-1 isolate – N-linked glycosylation modifications in the V2 loop of the SF162 gp120 revealed that these sites prevent neutralization by CD4BS MAbs (IgG1b12 and IgGCD4), and protect against neutralization by V3 MAbs (447-D and 391–95D) – V2-region glycosylation site mutations did not enhance neutralization resistance to V2 MAbs (G3.4 and G3.136) or CD4i MAbs (17b and 48d) – V2 glycosylation site modification allows increased infection of macrophages, probably due to glycosylated forms requiring fewer CCR5 molecules for viral entry [Ly & Stamatatos(2000)]
- IgG1b12: 26 HIV-1 group M isolates (clades A to H) were tested for binding to 47 MAbs, including 6 CD4BS MAbs – CD4BS MAbs bound consistently to most isolates of clade D, but poorly to isolates of other clades with the exception of broadly reactive MAb IgG1b12, binding to 22 of 26 isolates tested – 8 MAbs were tested for neutralization and MAb IgG1b12 was most potent, with 90% neutralization of 3/5 isolates tested [Nyambi (2000)]
- IgG1b12: Fab b12 was used – six mutations in MN change the virus from a high-infectivity neutralization resistant phenotype to low-infectivity neutralization sensitive – V3, CD4BS, and CD4i MAbs are 20–100 fold more efficient at neutralizing the sensitive form – the mutation L544P reduced binding of all MAbs against gp120 by causing conformational changes [Park (2000)]
- IgG1b12: Mutations in two glcosylation sites in the V2 region of HIV-1 ADA at positions 190 and 197 (187 DNTSYRLINCNTS) cause the virus to become CD4-independent and able to enter cells through CCR5 alone – these same mutations tended to increase the neutralization sensitivity of the virus, except the mutation 197 S/R which resulted in a carbohydrate addition to 195 N that disrupts the IgG1b12 binding site [Kolchinsky (2001)]
- IgG1b12: This paper describes the technical aspects of the crystallization of b12 at a resolution of 2.7 angstroms with all 12 Ig domains resolved [Saphire (2001a)]
- IgG1b12: This paper describes the biological implications of the crystal structure of b12 – a remarkable feature of this antibody is a long protruding finger-like CDR H3 that can dock in the recessed CD4-binding site – a contact residues in gp120 are modeled, with numbering based on the variable loop-deleted crystal structure of gp120 [Saphire (2001b)]
- IgG1b12: Primary isolates YU2 and ADA are more resistant to IgG1b12 neutralization than HXBc2: 90% Neutralization of HXBc2 is observed with 1.25 ug of IgG1b12, while ADA and YU2 require 2.5 and 5 ug respectively to achieve 50% neutralization, and 90% neutralization could not be achieved with 10 or 20 ug of IgG1b12, respectively [Yang (2001)]

- IgG1b12: Abs against the V3 loop (50.1, 58.2, 59.1, 257-D, 268-D, 447-52D), CD4BS (IgG1b12, 559–64D, F105), CD4i (17b), and to gp41 (2F5, F240) each showed similar binding efficiency to Env derived from related pairs of primary and TCLA lines (primary: 168P and 320SI, and TCLA: 168C and 320SI-C3.3), but the TCLA lines were much more susceptible to neutralization suggesting that the change in TCLA lines that make them more susceptible to NAbs alters some step after binding [York (2001)]
- IgG1b12: b12 recognizes a conformational epitope that overlaps with the CD4 binding site – a phage displayed peptide library was used to identify a peptide which bound b12, called B2.1, which competes with b12 in competition assays – B2.1 has significant homology to the D loop of gp120: upper case letters indicate residues B2.1 shares with gp120, heRsymFSDlenrcI – one of the goals of defining peptide mimics to the b12 epitope is to develop an immunogen that can stimulate b12-like antibodies, but B2.1 cross-linked to phage and ovalbumin bound IgG1b12 did not elicit cross-reactive gp120 Abs in mice or rabbits [Zwick (2001a)]
- IgG1b12: This paper primarily concerns 4E10 and Z13, MAbs that both bind proximally to the 2F5 binding site to a conserved epitope, and that neutralize some primary isolates from clades B, C, and E – broadly neutralizing MAbs 2F5, IgG1b12, and 4E10 and Z13 fail to neutralize different subsets of viruses [Zwick (2001b)]
- IgG1b12: Neutralization synergy between anti-HIV NAbs b12, 2G12, 2F5, and 4E10 was studied – a classic fixed-ratio method was used, as well as a method where one Ab was fixed at a low neutralization titer and the other was varied – using primary isolates, a two-four fold enhancement of neutralization was observed with MAb pairs, and a ten-fold enhancement with a quadruple Ab combination – no synergy was observed with any MAb pair in the neutralization of TCLA strain HXB2 – whole IgG1b12 and b12 Fab fragments behaved similarly in the neutralization assays – there was no evidence for cooperativity of binding between b12 and 2G12 to envelope spikes expressed on the cell surface of TCLA or primary isolates [Zwick (2001c)]
- IgG1b12: Intravenous passive transfer of MAb b12 provides dose-dependent protection from infection to macaques vaginally challenged with the R5 virus SHIV(162P4) – the primary isolate HIV-1SF162 is neutralized 90% (IC90) by b12 at 2 µg/ml, and SHIV162P4, derived from HIV-1SF162, was neutralized by 90% at 2 µg/ml in PHA-activated PBMC from rhesus macaques – the 90% neutralization titers achieved in three groups of animals that were given 25-, 5-, and 1-mg/kg doses were approximately 1:400, 1:80, and 1:16, respectively – the half-life of IgG1 b12 in plasma was about 1 week, but while the peak b12 plasma concentration was immediately after the infusion, the peak vaginal fluid concentration was 7–14 days later [Parren2001]
- IgG1b12: Structural aspects of the interaction of neutralizing Abs with HIV-1 Env are reviewed – Env essentially has three faces, one is largely inaccessible on the native trimer, and two that exposed but have low immunogenicity on primary viruses – neutralization is suggested to occur by inhibition of the interaction between gp120 and the target cell membrane receptors as a result of steric hindrance and it is noted that the attachment of approximately 70 IgG molecules per virion is required for neutralization, which is equivalent to about one IgG molecule per spike – the 2G12, 17b and b12 epitopes are discussed in detail – the structure of CD4-bound gp120 reveals features that HIV has evolved to escape anti-CD4BS Abs like IgG1b12 despite profound functional constraints – CD4BS Abs must first access the CD4 binding site, deeply recessed within the gp120 core, and the Fab of an Ab molecule is “wider” than CD4, and in addition the binding site is flanked by variable and glycosylated regions [Poignard (2001)]
- IgG1b12: Neutralizing synergy between MAbs 1b12, 2G12 and 2F5 was studied using surface plasmon resonance to determine the binding kinetics for these three MAbs with respect to monomeric and oligomeric env protein gp160 IIIB – the 2G12 epitope is highly accessible on both monomeric and oligomeric Envs, 1b12 is highly accessible on monomers but not oligomers, and 2F5 on neither form – binding of 2G12 exposes the 2F5 epitope on gp160 oligomers [Zeder-Lutz (2001)]

- IgG1b12: A luciferase-reporter gene-expressing T-cell line was developed to facilitate neutralization and drug-sensitivity assays – luciferase and p24 antigen neutralization titer end points were found comparable using NAb from sera from HIV+ donors, and MAbs 2F5, 2G12 and IgG1b12 [Spenlehauer (2001)]
- IgG1b12: A panel of 12 MAbs was used to identify those that could neutralize the dual-tropic primary isolate HIV-1 89.6 – six gave significant neutralization at 2 to 10 μg/ml: 2F5, 50–69, IgG1b12, 447-52D, 2G12, and 670-D – six did not have neutralizing activity: 654-D, 4.8D, 450-D, 246-D, 98–6, and 1281 – no synergy, only additive effects were seen for pairwise combinations of MAbs, and antagonism was noted between gp41 M Abs 50–69 and 98–6, as well as 98–6 and 2F5 [Verrier (2001)]
- IgG1b12: A combination of MAbs IgG1b12, 2F5, and 2G12 was given postnatally to four neonate macaques that were then challenged with highly pathogenic SHIV89.6P – one of the four infants remained uninfected after oral challenge, two infants had no or a delayed CD4(+) T-cell decline – the most potent combination included IgG1b12, which alone does not neutralize SHIV89.6P [Hofmann-Lehmann (2001)]
- IgG1b12: Twenty HIV clade C isolates from five different countries were susceptible to neutralization by anti-clade B MAbs in a synergistic quadruple combination of mAbs IgG1b12, 2G12, 2F5, and 4E10 [Xu (2001)]
- IgG1b12: Oligomeric gp140 (o-gp140) derived from R5 primary isolate US4 was characterized for use as a vaccine reagent – antigen capture ELISA was used to compare the antigenicity of gp120 and o-gp140 using a panel of well characterized MAbs – Abs directed against the CD4 binding site (IgGCD4 and IgG1b12) reacted slightly more strongly with the gp120 monomer than with the oligomer, as did sCD4 [Srivastava (2002)]
- IgG1b12: UK Medical Research Council AIDS reagent: ARP3065
- IgG1b12: NIH AIDS Research and Reference Reagent Program: 2640

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758 IgGCD4 (IgG-CD4) Env(dis) gp120(dis) human(IgG)

Ab type: CD4BS **Donor:** Genetech
References: [Capon (1989), Stamatatos & Cheng-Mayer(1998), Ly & Stamatatos(2000), Srivastava (2002)]

- IgGCD4: An antibody-like immunoadhesins molecule was constructed incorporating the gp120-binding domain of CD4 [Capon (1989)]
- IgGCD4: Deleting the V2 loop of neutralization-resistant HIV-1 isolate SF162 does not abrogate its replication in PBMC or macrophages, but it enhances its neutralization sensitivity to sera from patients with B clade infection up to 170-fold, and also enhances sensitivity to sera from clades A through F – deletion of V2 but not V1 slightly enhanced neutralization by CD4BS MAb IgGCD4 [Stamatatos & Cheng-Mayer(1998)]
- IgGCD4: SF162 is a neutralization-resistant HIV-1 isolate – N-linked glycosylation modifications in the V2 loop of the SF162 gp120 revealed that these sites prevent neutralization by CD4BS MAbs (IgG1b12 and IgGCD4), and protect against neutralization by V3 MAbs (447-D and 391–95D) – V2-region glycosylation site mutations did not alter neutralization resistance to V2 MAbs (G3.4 and G3.136) or CD4i MAbs (17b and 48d) – V2 glycosylation site modification allows infection of macrophages, probably due to glycosylated forms requiring fewer CCR5 molecules for viral entry [Ly & Stamatatos(2000)]

- IgGCD4: Oligomeric gp140 (o-gp140) derived from R5 primary isolate US4 was characterized for use as a vaccine reagent – antigen capture ELISA was used to compare the antigenicity of gp120 and o-gp140 using a panel of well characterized MAbs – Abs directed against the CD4 binding site (IgGCD4 and IgG1b12) reacted slightly more strongly with the gp120 monomer than with the oligomer, as did sCD4 [Srivastava (2002)]

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759 L28 Env(dis) gp120(dis) L HIV-1 infection human(IgG1κ)
Ab type: CD4BS **References:** [Ditzel (1995)]
- L28: Substitutions at 257 T/R, 368 D/R, 370 E/R and 370 E/Q, 475 M/S 102 E/L and 463 N/D reduce binding – binding was enhanced by removal of the V3 loop and by substitutions 45 W/S, 298 R/G, 381 E/P, 382 F/L, 420 I/R, 435 Y/H or Y/R – binding is sensitive to deglycosylation – heavy and light chain variable region sequence is available [Ditzel (1995)]

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760 L33 Env(dis) gp120(dis) L HIV-1 infection human(IgG1κ)
Ab type: CD4BS **References:** [Ditzel (1995)]
- L33: binding is sensitive to deglycosylation – heavy and light chain variable region sequence is available [Ditzel (1995)]

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761 L41 Env(dis) gp120(dis) L HIV-1 infection human(IgG1κ)
Ab type: CD4BS **References:** [Ditzel (1995)]
- L41: Substitutions at 133 D/R, 256 S/Y, 257 T/R, 368 D/R or D/T, 370 E/Q or E/R, 384 Y/E, and 421 K/L reduce binding – this Fab was retrieved from the library after masking with known anti-CD4BS MAbs – binding is sensitive to deglycosylation – heavy and light chain variable region sequence is available [Ditzel (1995)]

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762 L42 Env(dis) gp120(dis) L HIV-1 infection human(IgG1κ)
Ab type: CD4BS **References:** [Ditzel (1995)]
- L42: Substitutions at 257 T/R, 368 D/R, 370 E/R, 266 A/E and 477 D/V reduce binding – binding was significantly enhanced by 381 E/P and 382 F/L – binding is sensitive to deglycosylation – heavy and light chain variable region sequence is available [Ditzel (1995)]

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763 L52 Env(dis) gp120(dis) L HIV-1 infection human(IgG1κ)
Ab type: CD4BS **References:** [Ditzel (1995)]
- L52: Binding is sensitive to deglycosylation – heavy and light chain variable region sequence is available [Ditzel (1995)]

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764 L72 Env(dis) gp120(dis) murine( )
Ab type: CD4BS **Donor:** Dr. Hariharam, IDEC Pharmaceuticals Corp La Jolla, CA
References: [Ditzel (1997)]
- L72: Used to bind gp120 to solid phase to select MAbs from a phage selection library [Ditzel (1997)]

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765 M12 Env(dis) gp120(dis IIIB) L Vaccine murine(IgG)
Vaccine: *Vector/type:* vaccinia *Strain:* IIIB *HIV component:* oligomeric gp140
Ab type: CD4BS **Donor:** P. Earl, National Institute of Allergy and Infectious Diseases, NIH, Bethesda, MD
References: [Earl (1994), Sugiura (1999)]
- M12: There is a p15 gag specific MAb also named M12

- M12: A comparison of 25 gp120 specific, conformation dependent MAbs was done – M12 is part of a group of MAbs labeled A1 – all A1 MAbs were broadly cross-reactive with gp160 from B-clade R5, X4, and R5X4 viruses, blocked CD4 binding, were sensitive to mutations in gp120 positions 368 and 370 that directly contact CD4 – 50% neutralization of NL4–3 was achieved with 21 μg/ml of M12 [Sugiura (1999)]

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766 M13 Env(dis) gp120(dis IIIB) L Vaccine murine(IgG)

Vaccine: *Vector/type:* vaccinia *Strain:* IIIB *HIV component:* oligomeric gp140

Ab type: CD4BS **Donor:** P. Earl, National Institute of Allergy and Infectious Diseases, NIH, Bethesda, MD
References: [Earl (1994), Sugiura (1999)]

- M13: A comparison of 25 gp120 specific, conformation dependent MAbs was done – M13 is part of a group of MAbs labeled A1 – all A1 MAbs were broadly cross-reactive with gp160 from B-clade R5, X4, and R5X4 viruses, blocked CD4 binding, were sensitive to mutations in gp120 positions 368 and 370 that directly contact CD4 – 50% neutralization of NL4–3 was achieved with 35 μg/ml of M13 [Sugiura (1999)]

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767 M6 Env(dis) gp120(dis IIIB) no Vaccine murine(IgG)

Vaccine: *Vector/type:* vaccinia *Strain:* IIIB *HIV component:* oligomeric gp140

Ab type: CD4BS **Donor:** P. Earl, National Institute of Allergy and Infectious Diseases, NIH, Bethesda, MD
References: [Earl (1994), Sugiura (1999)]

- M6: A comparison of 25 gp120 specific, conformation dependent MAbs was done – M6 is part of a group of MAbs labeled A1 – all A1 MAbs were broadly cross-reactive with gp160 from B-clade R5, X4, and R5X4 viruses, blocked CD4 binding, were sensitive to mutations in gp120 positions 368 and 370 that directly contact CD4 [Sugiura (1999)]

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768 MAG 116 Env(dis) gp120(dis) L Vaccine murine( )

Vaccine: *Vector/type:* sCD4-gp120 complex *Strain:* HXB2 *HIV component:* gp120

Ab type: CD4BS **Donor:** C. Y. Kang, IDEC Inc
References: [Kang (1994)]

- MAG 116: Amino acid substitutions that reduce binding 10 fold: 256 S/Y, 257 T/R, 368 D/R or T, 370 E/R or Q, 384 Y/E, 421 K/L – neutralizes MN, IIIB and RF [Kang (1994)]

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769 MAG 12B Env(dis) gp120(dis) L Vaccine murine( )

Vaccine: *Vector/type:* sCD4-gp120 complex *Strain:* HXB2 *HIV component:* gp120

Ab type: CD4BS **Donor:** C. Y. Kang, IDEC Inc
References: [Kang (1994)]

- MAG 12B: Amino acid substitutions that reduce binding 10 fold: 257 T/R, 368 D/R or T, 370 E/R or Q, 384 Y/E, 477 D/V – weak neutralization of IIIB [Kang (1994)]

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770 MAG 29B Env(dis) gp120(dis) L Vaccine murine( )

Vaccine: *Vector/type:* sCD4-gp120 complex *Strain:* HXB2 *HIV component:* gp120

Ab type: CD4BS **Donor:** C. Y. Kang, IDEC Inc
References: [Kang (1994)]

- MAG 29B: Amino acid substitutions that reduce binding 10 fold: 257 T/R, 368 D/R or T, 370 E/R or Q, 384 Y/E, 386 N/Q, 421 K/L – weak neutralization of IIIB [Kang (1994)]

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771 MAG 3B Env(dis) gp120(dis) no Vaccine murine( )

Vaccine: *Vector/type:* sCD4-gp120 complex *Strain:* HXB2 *HIV component:* gp120

Ab type: CD4BS **Donor:** C. Y. Kang, IDEC Inc
References: [Kang (1994)]

- MAG 3B: Amino acid substitutions that reduce binding 10 fold: 256 S/Y, 257 T/R or A or G, 262 N/T, 368 D/R or T, 370 E/R or Q, 381 E/P, 384 Y/E, 421 K/L, 475 M/S, 477 D/V [Kang (1994)]

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772 MAG 55 (#55) Env(dis) gp120(dis) L Vaccine murine( )

Vaccine: *Vector/type:* sCD4-gp120 complex *Strain:* HXB2 *HIV component:* gp120

Ab type: CD4BS **Donor:** C. Y. Kang, IDEC Inc
References: [Kang (1994), Moore & Sodroski(1996)]

- MAG 55: Amino acid substitutions that reduce binding 10 fold: 256 S/Y, 257 T/R, 368 D/R or T, 370 E/R or Q, 384 Y/E, 421 K/L, 470 P/L, 475 M/S, 477 D/V – neutralizes MN, IIIB and RF [Kang (1994)]
- MAG 55: Called #55 – binding reciprocally inhibited by other anti-CD4 binding site MAbs, and by some C1-C5 MAbs – binding enhanced by anti-V3 MAb 110.5 and anti-V2 MAbs G3-136 and G3-4 – enhances binding of many anti-V3 and -V2 MAbs. [Moore & Sodroski(1996)]

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773 MAG 72 (L72) Env(dis) gp120(dis) L Vaccine murine( )

Vaccine: *Vector/type:* sCD4-gp120 complex *Strain:* HXB2 *HIV component:* gp120

Ab type: CD4BS **Donor:** C. Y. Kang or Dr. Hariharam, IDEC Pharmaceuticals Corp, La Jolla, CA
References: [Kang (1994), Ditzel (1997)]

- MAG 72: Amino acid substitutions that reduce binding 10 fold: 257 T/R or A or G, 262 N/T, 368 D/R or T, 370 E/R or Q, 384 Y/E, 421 K/L, 477 D/V – neutralizes MN, IIIB and RF [Kang (1994)]
- MAG 72: Called L72 – used to bind gp120 to solid phase to select MAbs from a phage selection library [Ditzel (1997)]

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774 MAG 86 Env(dis) gp120(dis) L Vaccine murine( )

Vaccine: *Vector/type:* sCD4-gp120 complex *Strain:* HXB2 *HIV component:* gp120

Ab type: CD4BS **Donor:** C. Y. Kang, IDEC Inc
References: [Kang (1994)]

- MAG 86: Amino acid substitutions that reduce binding 10 fold: 256 S/Y, 257 T/R, 368 D/R or T, 370 E/R or Q, 384 Y/E, 421 K/L, 470 P/L, 477 D/V – neutralizes MN, IIIB and RF [Kang (1994)]

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775 MAG 96 Env(dis) gp120(dis) L Vaccine murine( )

Vaccine: *Vector/type:* sCD4-gp120 complex *Strain:* HXB2 *HIV component:* gp120

Ab type: CD4BS **Donor:** C. Y. Kang, IDEC Inc
References: [Kang (1994)]

- MAG 96: Amino acid substitutions that reduce binding 10 fold: 256 S/Y, 257 T/R, 368 D/R or T, 370 E/R – weak neutralization of IIIB [Kang (1994)]

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776 MTW61D Env(dis) gp120(dis W61D) L HIV-1 infection human( )

Ab type: CD4BS **References:** [Sullivan (1998a)]

- MTW61D – the HIV-1 virus YU2 entry can be enhanced by MAbs binding to the CD4BS, V3 loop, and CD4i epitopes – the activation for this enhanced entry state could be conferred on HxB2 by introducing the YU2 V3 loop, or the YU2 V3 and V1/V2 loops – a similar effect is observed by sub-neutralizing concentrations of sCD4 and the effect is dependent of CCR5 – Fab fragment MTW61D also enhances YU2 entry, ruling out Fc interactions or Env cross-linking as a mechanism, while neutralizing HXBc2 – MTW61D was obtained by panning libraries derived from bone marrow from a long term asymptomatic donor against gp120 from primary isolate W61D [Sullivan (1998a)]

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777 S1–1 Env(dis) gp120(dis) L HIV-1 infection human(IgG1λ)

Ab type: CD4BS **References:** [Lake (1992), Moran (1993), Wisnewski (1996)]

- S1–1: Neutralizes IIIB and MN without complement, and neutralizes RF and a clinical isolate with complement – binds to native but not denatured gp120 – inhibits sCD4-gp120 binding [Lake (1992)]
- S1–1: Heavy (V HI) and light (V λIII) chain sequenced – no enhancing activity – similar germline sequence to MAb 86, but very different activity [Moran (1993)]
- S1–1: S1–1 is V H1 – V-region heavy chain usage was examined and a bias of enhanced V H1 and V H4, and reduced V H3, was noted among HIV infected individuals [Wisnewski (1996)]

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778 T13 Env(dis) gp120(dis IIIB) no Vaccine murine(IgG)

Vaccine: *Vector/type:* vaccinia *Strain:* IIIB *HIV component:* oligomeric gp140

Ab type: CD4BS **Donor:** P. Earl, National Institute of Allergy and Infectious Diseases, NIH, Bethesda, MD
References: [Earl (1994), Sugiura (1999)]

- T13: A comparison of 25 gp120 specific, conformation dependent MAbs was done – T13 is one of three MAbs labeled group Cb, that was type-specific for BH8 – T13 fully blocked CD4 binding, and the deletion of the V3 loop enhanced binding 10-fold [Sugiura (1999)]

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779 T49 Env(dis) gp120(dis IIIB) no Vaccine murine(IgG)

Vaccine: *Vector/type:* vaccinia *Strain:* IIIB *HIV component:* oligomeric gp140

Ab type: CD4BS **Donor:** P. Earl, National Institute of Allergy and Infectious Diseases, NIH, Bethesda, MD
References: [Earl (1994), Sugiura (1999)]

- T49: A comparison of 25 gp120 specific, conformation dependent MAbs was done – T49 is one of three MAbs labeled group Cb, that was type-specific for BH8 – T49 fully blocked CD4 binding, and the deletion of the V3 loop enhanced binding 10-fold [Sugiura (1999)]

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780 T56 Env(dis) gp120(dis IIIB) no Vaccine murine(IgG)

Vaccine: *Vector/type:* vaccinia *Strain:* IIIB *HIV component:* oligomeric gp140

Ab type: CD4BS **Donor:** P. Earl, National Institute of Allergy and Infectious Diseases, NIH, Bethesda, MD
References: [Earl (1994), Sugiura (1999)]

- T56: A comparison of 25 gp120 specific, conformation dependent MAbs was done – T56 is one of three MAbs labeled group Cb, that was type-specific for BH8 – T56 fully blocked CD4 binding, and the deletion of the V3 loop enhanced binding 10-fold [Sugiura (1999)]

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781 TH9 Env(dis) gp120(dis) L human(IgG1κ)

Ab type: CD4BS **Donor:** Michael Fung, Tanox Biosystem, USA
References: [D'Souza (1995), Yang (1998)]

- TH9: Found to neutralize MN, but not JRCSF, two B subtype primary isolates, or a D subtype primary isolate, by most labs in a multi-laboratory study involving 11 labs[D'Souza (1995)]
- TH9: A neutralization assay was developed based on hemi-nested PCR amplification of the LTR (HNPCR) – LTR-HNPCR consistently revealed HIV DNA and was shown to be a rapid, specific and reliable neutralization assay based on tests with 6 MAbs and 5 isolates [Yang (1998)]

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782 D33 Env(dis) gp120(dis IIIB) Vaccine murine(IgG)

Vaccine: *Vector/type:* vaccinia *Strain:* IIIB *HIV component:* oligomeric gp140

Ab type: CD4BS, C-term, N-term **Donor:** P. Earl, National Institute of Allergy and Infectious Diseases, NIH, Bethesda, MD
References: [Earl (1994), Sugiura (1999)]

- D33: A comparison of 25 gp120 specific, conformation dependent MAbs was done – D33 is part of a group of MAbs labeled A1 – all A1 MAbs were broadly cross-reactive with gp160 from B-clade R5, X4, and R5X4 viruses, blocked CD4 binding, were sensitive to mutations in gp120 positions 368 and 370 that directly contact CD4 – D33 was unusual for the group of A1 MAbs, because while it blocked CD4 binding completely, but competed with MAbs that did not in a BIAcore assay – both the N- and C-terminal ends of gp120 are involved in D33 binding [Sugiura (1999)]

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783 Env(dis) gp120(dis) yes human( )

Ab type: CD4BS, CD4i, V3, V2 **References:** [Moore (2001)]

- Moore and colleagues review structural aspects of gp120 and how they relate to antigenic domains, and review the data concerning the lack of a clear relationship between genetic subtype and serotype – they suggest the primary goal in vaccine efforts should be to design an immunogen that can be shown to elicit neutralizing antibodies against a significant proportion of primary isolates – assay artifacts that can result in confused interpretations are also discussed, such as Ab binding to defective spikes, which does not affect HIV-1 infectivity, but can dominant an assay signal [Moore (2001)]

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784 17b Env(dis conserved regions in gp120) gp120(dis) L P (weak) HIV-1 infection human( )

Ab type: CD4i **Donor:** J. Robinson

References: [Thali (1993), Moore (1993c), Thali (1994), Beretta & Dalgleish(1994), Wyatt (1995), Sattentau & Moore(1995), Moore & Sodroski(1996), Poignard (1996a), Wu (1996), Trkola (1996a), Binley (1997a), Fouts (1997), Li (1997), Weinberg (1997), Ditzel (1997), Cao (1997), Wyatt (1997), Parren (1997b), Kwong (1998), Wyatt (1998), Moore & Binley(1998), Rizzuto (1998), Sullivan (1998b), Sullivan (1998a), Binley (1998), Stamatatos & Cheng-Mayer(1998), Oscherwitz (1999), Hoffman (1999), Binley (1999), Grovit-Ferbas (2000), Ly & Stamatatos(2000), Park (2000), Salzwedel (2000), Stamatatos (2000), Kolchinsky (2001), York (2001), Zhang (2001), Poignard (2001), Srivastava (2002)]

- 17b: 48d and 17b have similar epitopes, and the pair are unique among human and rodent MAbs
- 17b: Epitope is better exposed upon CD4 binding to gp120 – competes with 15e and 21h, anti-CD4 binding site MAbs – 113 D/R, 252 R/W, 257 T/A or G, 370 E/D, 382 F/L, 420 I/R, 433A/L, 438 P/R and 475 M/S confer decreased sensitivity to neutralization [Thali (1993)]
- 17b: Binding of 48d is much more influenced by sequence variation among molecular clones of LAI than is binding of 17b [Moore (1993c)]
- 17b: A mutation in gp41, 582 A/T, confers resistance to neutralization (also confers resistance to MAbs F105, 48d, 21h and 15e) [Thali (1994)]
- 17b: Studies using a V1/V2 deletion mutant demonstrated that enhanced binding of 17b in the presence sCD4 involves the V1/V2 loops, with more significant involvement of V2 – similar effect observed for 48d and A32 [Wyatt (1995)]
- 17b: Binds with higher affinity to monomer and oligomer, slow association rate, poor neutralization of lab strain – this is in contrast to 48d, which has very different kinetics [Sattentau & Moore(1995)]
- 17b: Many MAbs inhibit binding (anti-C1, -C5, -C4, -CD4BS) – anti-V3 MAb 5G11 enhances binding, as do C1-C4 discontinuous epitopes A32 and 2/11c – enhances binding of some anti-V2 MAbs [Moore & Sodroski(1996)]
- 17b: Binding did not result in significant gp120 dissociation from virion, in contrast to 48d, although the the gp41 epitope of MAb 50–69 was exposed [Poignard (1996a)]
- 17b: MIP-1α binding to CCR-5 expressing cells can be inhibited by gp120-sCD4 – binding of 17b blocks this inhibition [Wu (1996)]
- 17b: Neutralizes JR-FL – inhibits gp120 interaction with CCR-5 in a MIP-1β-CCR-5 competition study [Trkola (1996a)]
- 17b: Study shows neutralization is not predicted by MAb binding to JRFL monomeric gp120, but is associated with oligomeric Env binding – 17b bound monomer, oligomer, and neutralized JRFL in the presence of sCD4, but if sCD4 was not present, 17b only bound monomer [Fouts (1997)]
- 17b: One of 14 human MAbs tested for ability to neutralize a chimeric SHIV-vpu+, which expressed HIV-1 IIIB env – 17b has synergistic response in combination with anti-V3 MAb 694/98-D [Li (1997)]
- 17b: 48d binds to the IIIB protein and not IIIB V3 peptide, while binding to the Can0A V3 peptide, suggesting Can0A V3 is a conformer that mimics the 48d – it does not bind to 17b, distinguishing the epitopes [Weinberg (1997)]
- 17b: Virus with the V1-V2 loop deleted was viable and more susceptible to neutralization by CD4i MAb 17b, and anti-V3 MAbs 1121, 9284, and 110.4, but not to a CD4BS MAb, F105, or sCD4 [Cao (1997)]

- 17b: Binds to sgp120 efficiently, but not soluble gp120+gp41, suggesting its gp120 epitope is blocked by gp41 binding – partial reexposure if sCD4 was bound – could not bind to HXBc2 gp120 if the 19 C-term amino acids were deleted in conjunction with amino acids 31–93 in C1, but binding was restored in the presence of sCD4 [Wyatt (1997)]
- 17b: Neutralizes TCLA strains, but not primary isolates [Parren (1997b)]
- 17b: 17b Fab was co-crystallized with a gp120 core and CD4, and it's binding site can be directly visualized – 17b binds to the "bridging sheet" of gp120, an antiparallel beta sheet region, contacting residues from the C4 region and the V1/V2 stem – the contact area is small for an Ab-antigen interactive surface, and dominated in the Ab by the heavy chain – the center of the binding region has hydrophobic interactions, and the periphery charge interactions, acidic on 17b and basic on gp120 [Kwong (1998)]
- 17b: Summary of the implications of the crystal structure of a gp120 core bound to CD4 and 17b, combined with what is known about mutations that reduce NAb binding to gp120 – probable mechanism of neutralization is interference with chemokine receptor binding – mutations in 88N, 117K, 121K, 256S, 257T, N262, Δ V3, E370, E381, F 382, R 419, I 420, K 421, Q 422, I 423, W 427, Y 435, P 438, M 475 of HXBc2 (IIIB) reduce binding – the only variable residues in gp120 that contact 17b are 202T and 434M – the contact points for 17b with the crystallized incomplete gp120 are mostly in the heavy chain of the Ab, and there is a gap between 17b's light chain and the partial gp120 which may be occupied by the V3 loop in a complete gp120 molecule – the authors propose that the V2 and V3 loops may mask the CD4i Ab binding site, and that the V2 loop may be repositioned upon CD4 binding [Wyatt (1998)]
- 17b: Moore and Binley provide a commentary on the papers by [Rizzuto (1998)], [Wyatt (1998)] and [Kwong (1998)] – they point out 17b shares binding elements in gp120 with chemokine receptor molecules, and that CD4 needs to bind to gp120 first to make the 17b epitope accessible and it may be stericly blocked in the CD4 bound virus, thus making it a poor NAb for primary isolates [Moore & Binley(1998)]
- 17b: Site directed mutagenesis of a WU2 protein with the V1-V2 loops deleted revealed key residues for 17b-gp120 interaction and interaction of gp120 and CCR5 – mutations in residues that reduced 17b by 70% were R/D 419, I/R 420, Q/L 422, Y/S 435, I/S 423, K/D 121 and K/D 421– 17b can neutralize HIV-1 strains that use different chemokine receptors, supporting a common region in gp120 in chemokine-receptor interaction [Rizzuto (1998)]
- 17b: sCD4 induces 17b binding in primary isolates and TCLA strains – amino acids that reduce the efficiency of binding were determined and found also to compromise syncytia formation and viral entry – V1V2 deletion or sCD4 binding can expose the 17b epitope for both HXBc2 and macrophage tropic YU2 – neutralizing potency of 17b is probably weak due to poor exposure of the epitope – 17b epitope exposure upon sCD4 binding can occur over a wide range of temperatures, consistent with the energy of CD4 binding being sufficient to drive the V1/V2 loop into a new conformation [Sullivan (1998b)]
- 17b: The HIV-1 virus YU2 entry can be enhanced by MAbs binding to the CD4BS, V3 loop, and CD4i epitopes – the activation for this enhanced entry state could be conferred on HxB2 by introducing the YU2 V3 loop, or the YU2 V3 and V1/V2 loops, and the presence of V1/V2 increased the enhancement – a similar effect is observed by sub-neutralizing concentrations of sCD4 and the effect is dependent of CCR5 – 17b enhances YU2 enhanced viral entry 10-fold, whereas HXBc2 was neutralized [Sullivan (1998a)]
- 17b: A panel of MAbs was shown to bind with similar or greater affinity and similar competition profiles to a deglycosylated or variable loop deleted core gp120 protein (Δ V1, V2, and V3), thus such a core protein produces a structure closely approximating full length folded monomer – CD4i MAbs 17b and 48d bound better to the deleted protein than to wild type [Binley (1998)]

- 17b: Deleting the V2 loop of neutralization-resistant HIV-1 isolate SF162 does not abrogate its replication in PBMC or macrophages, but it enhances its neutralization sensitivity to sera from patients with B clade infection up to 170-fold, and also enhances sensitivity to sera from clades A through F – deletion of V2 but not V1 enabled neutralization by CD4i MAbs 17b and 48d [Stamatatos & Cheng-Mayer(1998)]
- 17b: A CD4-independent viral variant of IIIB, IIIBx, was generated on CXCR4-expressing cells – IIIBx exhibited greater exposure of the 17b and 48d epitopes and enhanced neutralization by CD4i MAbs and by polyclonal human sera – the 17b epitope has significant overlap with the CCR5 coreceptor binding site [Hoffman (1999)]
- 17b: The MAbs with the broadest neutralizing activity, IgG1b12, 2G12 and 2F5, all have high affinity for the native trimer, indicating that they were raised in an immune response to the oligomer on the virion surface rather than dissociated subunits – a disulfide linked gp120-gp41 (SOS gp140) was created to mimic the native conformation of Env and explore its potential as an immunogen – SOS gp140 is recognized by NAbs IgG1b12, 2G12, and CD4-IgG2, and also by anti-V3 MAbs 19b and 83.1 – SOSgp140 is not recognized by C4 region MAbs that neutralize only TCLA strains, G3-42 and G3-519 – nor did it bind C11, 23A, and M90, MAbs that bind to gp120 C1 and C5, where it interacts with gp41 – MAbs that bind CD4 inducible epitopes, 17b and A32 were very strongly induced by CD4 in SOS gp140 – anti-gp41 MAbs that bind in the region that interacts with gp120, 7B2, 2.2B, T4, T15G1 and 4D4, did not bind to SOSgp140, in contrast to 2F5, which binds to the only gp41 epitope that is well exposed in native gp120-gp41 complexes [Binley (1999)]
- 17b: To determine the antigenicity of virus killed by thermal and chemical inactivation, retention of conformation-dependent neutralization epitopes was examined, and exposure of CD4BS epitopes was found to be enhanced (MAbs IgG1b12, 205-46-9, and 205-43-1) – binding to 2G12 and 447-52D epitopes was essentially unaltered – the 17b CD4i epitope was also exposed [Grovit-Ferbas (2000)]
- 17b: SF162 is a neutralization-resistant HIV-1 isolate – N-linked glycosylation modifications in the V2 loop of the SF162 gp120 revealed that these sites prevent neutralization by CD4BS MAbs (IgG1b12 and IgGCD4), and protect against neutralization by V3 MAbs (447-D and 391–95D) – V2-region glycosylation site mutations did not alter neutralization resistance to V2 MAbs (G3.4 and G3.136) or CD4i MAbs (17b and 48d) – V2 glycosylation site modification allows infection of macrophages, probably due to glycosylated forms requiring fewer CCR5 molecules for viral entry [Ly & Stamatatos(2000)]
- 17b: Six mutations in MN change the virus from a high-infectivity neutralization resistant phenotype to low-infectivity neutralization sensitive – V3, CD4BS, and CD4i MAbs are 20–100 fold more efficient at neutralizing the sensitive form – the mutation L544P reduced binding of all MAbs against gp120 by causing conformational changes [Park (2000)]
- 17b: sCD4 can activate fusion between effector cells expressing Env and target cells expressing coreceptor (CCR5 or CXCR4) alone without CD4 – CD4i MAbs 17b and 48d have little effect on a standard cell fusion assay but potently block sCD4 activated fusion – 17b was broadly cross-reactive inhibiting sCD4 activated fusion with Env from clades A, B, C, D, E, F, and F/B [Salzwedel (2000)]
- 17b: Soluble gp140 derived from SF162, a neutralization-resistant primary isolate, and SF162AV2 a neutralization-susceptible isolate with 30 amino acids deleted from the V2 loop, were generated with or without the gp120-gp41 cleavage site intact – all forms are recognized by oligomer-specific MAb T4 and show enhanced binding of CD4i MAb 17b when sCD4 is bound – the fused forms are less efficiently recognized than the cleaved forms by polyclonal neutralizing sera from HIV-infected patients – the V3 loop is more exposed on the fused form [Stamatatos (2000)]

- 17b: Mutations in two glcosylation sites in the V2 region of HIV-1 ADA at positions 190 and 197 (187 DNTSYRLINCNTS 199) cause the virus to become CD4-independent and able to enter cells through CCR5 alone – these same mutations tended to increase the neutralization sensitivity of the virus, including to 17b – only the CD4i antibodies 17b and 48d showed an increased affinity of the CD4 independent viruses relative to wild-type [Kolchinsky (2001)]
- 17b: Abs against the V3 loop (50.1, 58.2, 59.1, 257-D, 268-D, 447-52D), CD4BS (IgG1b12, 559–64D, F105), CD4i (17b), and to gp41 (2F5, F240) each showed similar binding efficiency to Env derived from related pairs of primary and TCLA lines (primary: 168P and 320SI, and TCLA: 168C and 320SI-C3.3), but the TCLA lines were much more susceptible to neutralization suggesting that the change in TCLA lines that make them more susceptible to NAbs alters some step after binding – 17b bound at somewhat greater levels to 168C than to 168P, but this is not a general feature of 17b binding to primary versus TCLA strains [York (2001)]
- 17b: 17b binds to a CD4 inducible epitope which partially overlaps the CCR5 binding site – JRFL, YU2, 89.6, and HXB2 and their C1-, V1/V2-, C5 -deletion mutants were used to study how 17b binding affects gp120-CD4 interactions – 17b reduced CD4-gp120 interactions by decreasing the on-rate and increasing the off-rate of sCD4, while enhanced binding of sCD4 binding was observed for the 17b-bound, V1/V2 deleted gp120s – 17b was considered to be a surrogate for CCR5, and the authors suggest that 17b binding may shift V1/V2 into a position that interferes with CD4 binding, forcing a release [Zhang (2001)]
- 17b: Structural aspects of the interaction of neutralizing Abs with HIV-1 Env are reviewed – Env essentially has three faces, one is largely inaccessible on the native trimer, and two are exposed but have low immunogenicity on primary viruses – neutralization is suggested to occur by inhibition of the interaction between gp120 and the target cell membrane receptors as a result of steric hindrance and it is noted that the attachment of approximately 70 IgG molecules per virion is required for neutralization, which is equivalent to about one IgG molecule per spike – the 2G12, 17b and b12 epitopes are discussed in detail – the 17b epitope is masked prior to CD4 binding by the V1-V2 loop and in contrast to sCD4, the binding of cell surface CD4 to virus does not appear to make the epitope accessible to binding by 17b to allow neutralization [Poignard (2001)]
- 17b: Oligomeric gp140 (o-gp140) derived from R5 primary isolate US4 was characterized for use as a vaccine reagent – antigen capture ELISA was used to compare the antigenicity of gp120 and o-gp140 using a panel of well characterized MAbs – 17b recognized both gp120 monomer and o-gp140 [Srivastava (2002)]

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785 48d (4.8d, 4.8D) | Env(dis) | gp120(dis) | L P (weak) | HIV-1 infection | human(IgG1κ)

Ab type: CD4i **Donor:** J. Robinson, Tulane University, New Orleans, LA, USA
References: [Thali (1993), Moore & Ho(1993), Moore (1993c), Thali (1994), Moore (1994b), D'Souza (1995), Sattentau(1995), Wyatt (1995), Sattentau & Moore(1995), Moore & Sodroski(1996), Poignard (1996a), Trkola (1996a), Binley (1997a), Li (1997), Weinberg (1997), Lee (1997), Ugolini (1997), Wyatt (1997), Parren (1997b), Frankel (1998), Wyatt (1998), Mondor (1998), Parren (1998a), Sullivan (1998b), Yang (1998), Binley (1998), Stamatatos & Cheng-Mayer(1998), Oscherwitz (1999), Hoffman (1999), Fortin (2000), Ly & Stamatatos(2000), Park (2000), Salzwedel (2000), Kolchinsky (2001), Verrier (2001)]

- 48d: 48d and 17b have similar epitopes, and the pair are unique among human and rodent MAbs
- 48d: Epitope is better exposed upon CD4 binding to gp120 – competes with ICR 39.13, 15e and 21h, anti-CD4 binding site MAbs – inhibited by anti-CD4BS MAb ICR 39.13g and linear anti-C4 MAbs G3-42 and G3-508 – 113 D/R, 252 R/W, 257 T/A or G, 370 E/D, 382 F/L, 420 I/R, 421 K/L, 433A/L, 438 P/R and 475 M/S confer decreased sensitivity to neutralization [Thali (1993)]

- 48d: Called 4.8d – Neutralizes IIIB – reactive with SF-2 gp120 – does not inhibit HIV-1 sera from binding to IIIB gp120 [Moore & Ho(1993)]
- 48d: Binding of 48d is much more influenced by sequence variation among molecular clones of LAI than is binding of 17b [Moore (1993c)]
- 48d: A mutation in gp41, 582 A/T, confers resistance to neutralization (also confers resistance to MAbs F105, 21h, 15e and 17b) [Thali (1994)]
- 48d: Poor cross-reactivity with gp120 from most clades [Moore (1994b)]
- 48d: Called 4.8D – Found to neutralize MN, but not JRCSF, two B subtype primary isolates, or a D subtype primary isolate, by most labs in a multi-laboratory study involving 11 labs[D'Souza (1995)]
- 48d: Studies using a V1/V2 deletion mutant demonstrated that enhanced binding of 48d in the presence of sCD4 involves the V1/V2 loops, with more significant involvement of V2 – similar effect observed for 17b and A32 [Wyatt (1995)]
- 48d: Formalin inactivation of virus at 0.1% formalin for 10 hours at 4 degrees was optimal for inactivation of virus while maintaining epitope integrity [Sattentau (1995)]
- 48d: Binds with similar affinity to monomer and oligomer, moderate association rate, potent neutralization – this is in contrast to 17b, which has very different kinetics [Sattentau & Moore(1995)]
- 48d: Many MAbs inhibit binding (anti-C1, -C5, -C4, -CD4BS) – anti-C1-C4 discontinuous epitope MAbs A32 and 2/11c enhance binding – reciprocal enhanced binding with some anti-V2 MAbs [Moore & Sodroski(1996)]
- 48d: Binding resulted in gp120 dissociation from virion, mimicking sCD4, and exposure of the gp41 epitope of MAb 50–69, in contrast to CD4BS MAbs [Poignard (1996a)]
- 48d: Neutralizes JR-FL – slightly inhibits gp120 interaction with CCR-5 in a MIP-1β-CCR-5 competition study [Trkola (1996a)]
- 48d: One of 14 human MAbs tested for ability to neutralize a chimeric SHIV-vpu+, which expressed HIV-1 IIIB env – all Ab combinations tested showed synergistic neutralization – 48d has synergistic response with MAbs 694/98-D (anti-V3) and F105 [Li (1997)]
- 48d: 48d binds to the IIIB protein and not IIIB V3 peptide, while binding to the Can0A V3 peptide, suggesting Can0A V3 is a conformer that mimics the 48d, (but not 17b), epitope [Weinberg (1997)]
- 48d: Prefers CD4-gp120 complex to gp120 alone, but does not enhance fusion, in contrast to MAb CG10, in fact it inhibits syncytium formation [Lee (1997)]
- 48d: Viral binding inhibition by 48d was strongly correlated with neutralization (all other neutralizing MAbs tested showed some correlation except 2F5) [Ugolini (1997)]
- 48d: Binds efficiently to sgp120 but not soluble gp120+gp41, suggesting its gp120 epitope is blocked by gp41 binding [Wyatt (1997)]
- 48d: Neutralizes TCLA strains, but not primary isolates [Parren (1997b)]
- 48d: Summary of the implications of the crystal structure of the core of gp120 bound to CD4 and 17b with what is known about mutations that reduce NAb binding – probable mechanism of neutralization of 48d is interference with chemokine receptor binding – CD4 binding increases exposure of epitope due to V2 loop movement – 88N, 117K, 121K, 256S, 257T, N262, delta V3, E370, E381, F 382, R 419, I 420, K 421, Q 422, I 423, W 427, Y 435, P 438, M 475 mutations in HXBc2 (IIIB) decrease binding [Wyatt (1998)]
- 48d: Inhibits binding of Hx10 to both CD4 positive and CD4 negative HeLa cells [Mondor (1998)]
- 48d: The MAb and Fab binding to the oligomeric form of gp120 and neutralization were highly correlated – authors suggest that neutralization is determined by the fraction of Ab sites occupied on a virion irrespective of the epitope [Parren (1998a)]

- 48d: CD4i MAbs 17b and 48d compete with MAb CG10, and the binding sites may overlap – MAb A32 enhances binding of 17b, 48d and CG10 [Sullivan (1998b)]
- 48d: A neutralization assay was developed based on hemi-nested PCR amplification of the LTR (HNPCR) – LTR-HNPCR consistently revealed HIV DNA and was shown to be a rapid, specific and reliable neutralization assay based on tests with 6 MAbs and 5 isolates [Yang (1998)]
- 48d: A panel of MAbs were shown to bind with similar or greater affinity and similar competition profiles to a deglycosylated or variable loop deleted core gp120 protein (Δ V1, V2, and V3), thus such a core protein produces a structure closely approximating full length folded monomer – CD4i MAbs 17b and 48d bound better to the deleted protein than to wild type [Binley (1998)]
- 48d: Deleting the V2 loop of neutralization-resistant HIV-1 isolate SF162 does not abrogate its replication in PBMC or macrophages, but it enhances its neutralization sensitivity to sera from patients with B clade infection up to 170-fold, and also enhances sensitivity to sera from clades A through F – deletion of V2 but not V1 enabled neutralization by CD4i MAbs 17b and 48d [Stamatatos & Cheng-Mayer(1998)]
- 48d: Infection of dendritic cells cultured from CD14+ blood cells or from cadaveric human skin was blocked by neutraling MAbs IgG1b12, or 2F5 and 2G12 delivered together, but not by control non-neutralizing anti-gp120 MAb 4.8D, indicating that NAbs could interrupt early mucosal transmission events [Frankel (1998)]
- 48d: A CD4-independent viral variant of IIIB, IIIBx, was generated on CXCR4-expressing cells – IIIBx exhibited greater exposure of the 17b and 48d epitopes and enhanced neutralization by CD4i MAbs and by polyclonal human sera [Hoffman (1999)]
- 48d: Called 4.8D – host encoded intercellular adhesion molecule (ICAM-1) is incorporated by the HIV-1 virion and enhances viral infectivity – ICAM-1 does not modify virus sensitivity to antibodies 0.5β or 4.8D or sCD4, but neutralizing ability of F105 was diminished in ICAM bearing virions in the presence of lymphocyte function-association antigen-1 (LFA-1) Ab [Fortin (2000)]
- 48d: SF162 is a neutralization-resistant HIV-1 isolate – N-linked glycosylation modifications in the V2 loop of the SF162 gp120 revealed that these sites prevent neutralization by CD4BS MAbs (IgG1b12 and IgGCD4), and protect against neutralization by V3 MAbs (447-D and 391–95D) – V2-region glycosylation site mutations did not alter neutralization resistance to V2 MAbs (G3.4 and G3.136) or CD4i MAbs (17b and 48d) – V2 glycosylation site modification allows infection of macrophages, probably due to glycosylated forms requiring fewer CCR5 molecules for viral entry [Ly & Stamatatos(2000)]
- 48d: Six mutations in MN change the virus from a high-infectivity neutralization resistant phenotype to low-infectivity neutralization sensitive – V3, CD4BS, and CD4i MAbs are 20–100 fold more efficient at neutralizing the sensitive form – the mutation L544P reduced binding of all MAbs against gp120 by causing conformational changes [Park (2000)]
- 48d: sCD4 can activate fusion between effector cells expressing Env and target cells expressing coreceptor (CCR5 or CXCR4) alone without CD4 – CD4i MAbs 17b and 48d have little effect on a standard cell fusion assay but potently block sCD4 activated fusion [Salzwedel (2000)]
- 48d: Mutations in two glcosylation sites in the V2 region of HIV-1 ADA at positions 190 and 197 (187 DNTSYRLINCNTS 199) cause the virus to become CD4-independent and able to enter cells through CCR5 alone – these same mutations tended to increase the neutralization sensitivity of the virus, including to 48d – only the CD4i antibodies 17b and 48d showed an increased affinity of the CD4 independent viruses relative to wild-type [Kolchinsky (2001)]

- 48d: Called 4.8d – A panel of 12 MAbs was used to identify those that could neutralize the dual-tropic primary isolate HIV-1 89.6 – six gave significant neutralization at 2 to 10 μg/ml: 2F5, 50–69, IgG1b12, 447-52D, 2G12, and 670-D – six did not have neutralizing activity: 654-D, 4.8D, 450-D, 246-D, 98–6, and 1281 – no synergy, only additive effects were seen for pairwise combinations of MAbs, and antagonism was noted between gp41 MAbs 50–69 and 98–6, as well as 98–6 and 2F5 [Verrier (2001)]
- 48d: NIH AIDS Research and Reference Reagent Program: 1756

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786 A32 Env(dis) gp120(dis) no HIV-1 infection human(IgG1)
Ab type: CD4i **Donor:** J. Robinson, Tulane University, New Orleans, LA, USA
References: [Moore (1994b), Wyatt (1995), Moore & Ho(1995), Moore & Sodroski(1996), Wu (1996), Trkola (1996a), Binley (1997a), Fouts (1997), Burton & Montefiori(1997), Wyatt (1997), Boots (1997), Parren (1997b), Sullivan (1998b), Binley (1998), Binley (1999)]

- A32: Reacted with virtually every gp120 monomer of every clade tested, most conserved gp120 monomer epitope known [Moore (1994b)]
- A32: Epitope is better exposed upon CD4 binding to gp120 – binding of A32 enhances binding of 48d and 17b – studies using a V1/V2 deletion mutant demonstrated that enhanced binding of 48d in the presence sCD4 involves the V1/V2 loops, with more significant involvement of V2 [Wyatt (1995)]
- A32: Review: epitope is distinct from CD4BS MAbs, 48d and 17b, and 2G12 [Moore & Ho(1995)]
- A32: Reciprocal inhibition of binding of anti-C1, -C5, -C4, -V3 and anti-CD4 binding site MAbs – induces binding of some anti-V2 and sCD4 inducible MAbs (48d and 17b) – very similar competition pattern to 2/11c, A32 and 211/c are unique among known human and rodent MAbs [Moore & Sodroski(1996)]
- A32: Not neutralizing – binds domains that interact with gp41 – MIP-1α binding to CCR-5 expressing cells can be inhibited by gp120-sCD4 and binding of A32 does not block this inhibition [Wu (1996)]
- A32: Does not neutralize JR-FL, or any strain strongly – partial inhibition of gp120 interaction with CCR-5 in a MIP-1β-CCR-5 competition study [Trkola (1996a)]
- A32: Study shows neutralization is not predicted by MAb binding to JRFL monomeric gp120, but is associated with oligomeric env binding – A32 bound monomer, did not bind oligomer or neutralize JRFL [Fouts (1997)]
- A32: Review [Burton & Montefiori(1997)]
- A32: Binds efficiently to sgp120 but not soluble gp120+gp41, suggesting its gp120 epitope is blocked by gp41 binding [Wyatt (1997)]
- A32: Does not neutralize TCLA strains or primary isolates [Parren (1997b)]
- A32: Abs that recognize discontinuous epitopes can identify mimotopes from a phage peptide display library – A32 has a unique epitope involving mostly C2 but C1 and C4 contribute – six quite variable phage inserts were recognized, with a consensus of LPWYN – a central Trp was the most conserved element, consistent with W427 being an important residue for binding gp120 [Boots (1997)]
- A32: Enhances binding of CD4i MAbs 17b and 48d, and a MAb generated in response to gp120-CD4 complex CG10 [Sullivan (1998b)]
- A32: A panel of MAbs were shown to bind with similar or greater affinity and similar competition profiles to a deglycosylated or variable loop deleted core gp120 protein (Δ V1, V2, and V3), thus such a core protein produces a structure closely approximating full length folded monomer [Binley (1998)]

- A32: The MAbs with the broadest neutralizing activity, IgG1b12, 2G12 and 2F5, all have high affinity for the native trimer, indicating that they were raised in an immune response to the oligomer on the virion surface rather than dissociated subunits – a disulfide linked gp120-gp41 (SOS gp140) was created to mimic the native conformation of Env and explore its potential as an immunogen – SOS gp140 is recognized by NAbs IgG1b12, 2G12, and CD4-IgG2, and also by anti-V3 MAbs 19b and 83.1 – SOSgp140 is not recognized by C4 region MAbs that neutralize only TCLA strains, G3-42 and G3-519 – nor did it bind C11, 23A, and M90, MAbs that bind to gp120 C1 and C5, where it interacts with gp41 – MAbs that bind CD4 inducible epitopes, 17b and A32 were very strongly induced by CD4 in SOS gp140 – anti-gp41 MAbs that bind in the region that interacts with gp120, 7B2, 2.2B, T4, T15G1 and 4D4, did not bind to SOSgp140, in contrast to 2F5, which binds to the only gp41 epitope that is well exposed in native gp120-gp41 complexes [Binley (1999)]

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787 1367 | Env(dis gp41 567–647) | gp41(dis) | | HIV-1 infection | human(IgG1λ)

Ab type: cluster I **Donor:** Susan Zolla-Pazner (Zollas01@mcrcr6.med.nyu) (NYU Med. Center)
References: [Nyambi (1998), Gorny & Zolla-Pazner(2000), Gorny (2000), Nyambi (2000)]

- 1367: Using a whole virion-ELISA method, 18 human MAbs were tested for their ability to bind to a panel of 9 viruses from clades A, B, D, F, G, and H – anti-gp41 Abs 98–6, 1367 and 1342 were not able to bind detectably with any of the viruses from any clade [Nyambi (1998)]
- 1367: This antibody binds to acluster I epitope in rgp41, 567–647, and recognizes a peptide N51-C43 complex trimer of heterodimers that approximates the core of the fusogenic form of gp41 – this MAb doesn‘t react with either of the peptides N51 or C43 individually – MAbs 50–69 and 1367 had similar properties [Gorny & Zolla-Pazner(2000)]
- 1367: Binding of a panel of 21 MAbs to soluble oligomeric gp140 was compared to gp41 and gp120 monomers – no MAb was oligomer specific, but gp41 MAb 50–69 bound with a 5 fold preference for the oligomer, while other gp41 MAbs (1367, 98–6, 167-D, 1281, 1342, and 1379) did not show a preference [Gorny (2000)]
- 1367: 26 HIV-1 group M isolates (clades A to H) were tested for binding to 47 MAbs, including 5 cluster I anti-gp41 MAbs which showed good cross clade reactivity – 1367 weakly bound to the majority of isolates – no neutralizing activity was observed when tested with 5 isolates, but 1367 did not bind well to these isolates [Nyambi (2000)]

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788 126-6 (SZ-126.6) | Env( ) | gp41(HXB2) | no | HIV-1 infection | human(IgG2κ)

Ab type: cluster II **Donor:** Susan Zolla-Pazner (Zollas01@mcrcr6.med.nyu), NYU Med Center, NY, NY
References: [Robinson (1990b), Robinson (1991), Xu (1991), Eddleston (1993), Chen (1995), Binley (1996), Earl (1997), Gorny & Zolla-Pazner(2000), Nyambi (2000)]

- 126-6: No enhancing activity for HIV-1 IIIB [Robinson (1990b)]
- 126-6: No enhancing or neutralizing activity [Robinson (1991)]
- 126-6: Antibody is specific for a conformational epitope [Xu (1991)]
- 126-6: Called SZ-126.6 [Eddleston (1993)]
- 126-6: One of several anti-gp41 MAbs that bind to a gp41-maltose binding fusion protein designed to study the leucine zipper domain of gp41, showing that the construct has retained aspects of normal gp41 conformation [Chen (1995)]

- 126-6: Discontinuous epitope recognizing residues between 649–668 – designated cluster II – Fabs D5, D11, G1, T3, M12, M15, S6, S8, S9, S10 block binding [Binley (1996)]
- 126-6: This cluster II MAb binds to a conformational epitope in the region 644–663 – like most cluster II MAbs (126-6, 167-D, 1281, 1342, and 1379 all reacted similarly) it binds to a peptide N51-C43 complex trimer of heterodimers that approximates the core of the fusogenic form of gp41, but not to C43 nor to N51 alone – MAb 126-6 was biotinylated and used as a probe to determine that anti-gp41 MAb 50–69 bound the fusogenic form of the protein in liquid phase [Gorny & Zolla-Pazner(2000)]
- 126-6: 26 HIV-1 group M isolates (clades A to H) were tested for binding to 47 MAbs, including 6 cluster II anti-gp41 MAbs – of these 2F5, 167-D, 126-6, and 1281 bound across clades, but usually weakly, while 98–6 and 1342 had poor cross reactivity – Clade D isolates bound most consistently to cluster II MAbs [Nyambi (2000)]
- 126-6: NIH AIDS Research and Reference Reagent Program: 1243

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789 1281 Env(dis gp41 647–682) gp41(dis) HIV-1 infection human(IgG1λ)

Ab type: cluster II **Donor:** Susan Zolla-Pazner (Zollas01@mcrcr6.med.nyu) (NYU Med. Center)
References: [Gorny & Zolla-Pazner(2000), Gorny (2000), Verrier (2001)]

- 1281: This cluster II MAb binds to a conformational epitope in the region 644–663 – like most cluster II MAbs (126-6, 167-D, 1281, 1342, and 1379 all reacted similarly) it binds to a peptide N51-C43 complex trimer of heterodimers that approximates the core of the fusogenic form of gp41, but not to C43 nor to N51 alone [Gorny & Zolla-Pazner(2000)]
- 1281: Binds within the region gp41 647–682 – binding of panel of 21 MAbs to soluble oligomeric gp140 versus gp41 or gp120 monomers was compared – no MAb was oligomer specific, but gp41 MAb 50–69 bound with a 5 fold preference for the oligomer, while other gp41 MAbs (1367, 98–6, 167-D, 1281, 1342, and 1379) did not show a preference [Gorny (2000)]
- 246-D: A panel of 12 MAbs was used to identify those that could neutralize the dual-tropic primary isolate HIV-1 89.6 – six gave significant neutralization at 2 to 10 μg/ml: 2F5, 50–69, IgG1b12, 447-52D, 2G12, and 670-D – six did not have neutralizing activity: 654-D, 4.8D, 450-D, 246-D, 98–6, and 1281 – no synergy, only additive effects were seen for pairwise combinations of MAbs, and antagonism was noted between gp41 MAbs 50–69 and 98–6, as well as 98–6 and 2F5 [Verrier (2001)]

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790 1342 Env(dis 647–682) gp41(dis) no HIV-1 infection human(IgG1λ)

Ab type: cluster II **Donor:** Susan Zolla-Pazner (Zollas01@mcrcr6.med.nyu) (NYU Med. Center)
References: [Nyambi (1998), Gorny & Zolla-Pazner(2000), Gorny (2000), Nyambi (2000)]

- 1342: Using a whole virion-ELISA method, 18 human MAbs were tested for their ability to bind to a panel of 9 viruses from clades A, B, D, F, G, and H – anti-gp41 Abs 98–6, 1367 and 1342 were not able to bind detectably with any of the viruses from any clade [Nyambi (1998)]
- 1342: This cluster II MAb is a conformational epitope that binds in the region 644–663 – like most cluster II MAbs (126-6, 167-D, 1281, 1342, and 1379 all reacted similarly) it binds to a peptide N51-C43 complex trimer of heterodimers that approximates the core of the fusogenic form of gp41, but not to C43 nor to N51 alone [Gorny & Zolla-Pazner(2000)]
- 1342: Binds within the region gp41 647–682 – binding of panel of 21 MAbs to soluble oligomeric gp140 versus gp41 or gp120 monomers was compared – no MAb was oligomer specific, but gp41 MAb 50–69 bound with a 5 fold preference for the oligomer, while other gp41 MAbs (1367, 98–6, 167-D, 1281, 1342, and 1379) did not show a preference [Gorny (2000)]

- 1342: 26 HIV-1 group M isolates (clades A to H) were tested for binding to 47 MAbs, including 6 cluster II anti-gp41 MAbs – of these 2F5, 167-D, 126-6, and 1281 bound across clades, but usually weakly, while 98–6 and 1342 had poor cross reactivity – Clade D isolates bound most consistently to cluster II MAbs – no neutralizing activity was observed when tested with 5 isolates, but 1342 did not bind to these isolates [Nyambi (2000)]

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791 1379 Env(dis gp41 647–682) gp41(dis) HIV-1 infection human(IgG1λ)

Ab type: cluster II **Donor:** Susan Zolla-Pazner (Zollas01@mcrcr6.med.nyu) (NYU Med. Center)
References: [Gorny & Zolla-Pazner(2000), Gorny (2000)]

- 1379: This cluster II MAb binds to a conformational epitope in the region 644–663 – like most cluster II MAbs (126-6, 167-D, 1281, 1342, and 1379 all reacted similarly) it binds to a peptide N51-C43 complex trimer of heterodimers that approximates the core of the fusogenic form of gp41, but not to C43 nor to N51 alone [Gorny & Zolla-Pazner(2000)]
- 1379: Binds within the region gp41 647–682 – binding of panel of 21 MAbs to soluble oligomeric gp140 versus gp41 or gp120 monomers was compared – no MAb was oligomer specific, but gp41 MAb 50–69 bound with a 5 fold preference for the oligomer, while other gp41 MAbs (1367, 98–6, 167-D, 1281, 1342, and 1379) did not show a preference [Gorny (2000)]

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792 Fab D11 Env(dis) gp41(dis LAI) no HIV-1 infection human(IgG1κ)

Ab type: cluster II **References:** [Binley (1996)]

- Fab D11: Binds to cluster II region – competes with MAbs 126-6, Md-1 and D50 – conformation sensitive – variable regions sequenced [Binley (1996)]

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793 Fab D5 Env(dis) gp41(dis LAI) no HIV-1 infection human(IgG1κ)

Ab type: cluster II **References:** [Binley (1996)]

- Fab D5: Binds to cluster II region – competes with MAbs 126-6, Md-1 and D50 – conformation sensitive – variable regions sequenced [Binley (1996)]

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794 Fab G1 Env(dis) gp41(dis LAI) no HIV-1 infection human(IgG1κ)

Ab type: cluster II **References:** [Binley (1996)]

- Fab G1: Binds to cluster II region – competes with MAbs 126-6, Md-1 and D50 – conformation sensitive – variable regions sequenced [Binley (1996)]

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795 Fab M10 Env(dis) gp41(dis LAI) no HIV-1 infection human(IgG1κ)

Ab type: cluster II **References:** [Binley (1996), Parren (1997b)]

- Fab M10: Binds to cluster II region – competes with MAbs 126-6, Md-1 and D50 – conformation sensitive – variable regions sequenced [Binley (1996)]
- Fab M10: Does not bind to MN native oligomer, but does bind to both LAI and MN rgp120 and rgp140 [Parren (1997b)]

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796 Fab M12 Env(dis) gp41(dis LAI) no HIV-1 infection human(IgG1κ)

Ab type: cluster II **References:** [Binley (1996)]

- Fab M12: Binds to cluster II region – competes with MAbs 126-6, Md-1 and D50 – conformation sensitive – variable regions sequenced [Binley (1996)]

797	Fab M15	Env(dis)	gp41(dis LAI)	no	HIV-1 infection	human(IgG1κ)

Ab type: cluster II **References:** [Binley (1996)]

- Fab M15: Binds to cluster II region – competes with MAbs 126-6, Md-1 and D50 – conformation sensitive – variable regions sequenced [Binley (1996)]

798	Fab S10	Env(dis)	gp41(dis LAI)	no	HIV-1 infection	human(IgG1κ)

Ab type: cluster II **References:** [Binley (1996)]

- Fab S10: Binds to cluster II region – competes with MAbs 126-6, Md-1 and D50 – conformation sensitive – variable regions sequenced [Binley (1996)]

799	Fab S6	Env(dis)	gp41(dis LAI)	no	HIV-1 infection	human(IgG1κ)

Ab type: cluster II **References:** [Binley (1996)]

- Fab S6: Binds to cluster II region – competes with MAbs 126-6, Md-1 and D50 – conformation sensitive – variable regions sequenced [Binley (1996)]

800	Fab S8	Env(dis)	gp41(dis LAI)	no	HIV-1 infection	human(IgG1κ)

Ab type: cluster II **References:** [Binley (1996)]

- Fab S8: Binds to cluster II region – competes with MAbs 126-6, Md-1 and D50 – conformation sensitive – variable regions sequenced [Binley (1996)]

801	Fab S9	Env(dis)	gp41(dis LAI)	no	HIV-1 infection	human(IgG1κ)

Ab type: cluster II **References:** [Binley (1996)]

- Fab S9: Binds to cluster II region – competes with MAbs 126-6, Md-1 and D50 – conformation sensitive – variable regions sequenced [Binley (1996)]

802	Fab T3	Env(dis)	gp41(dis LAI)	no	HIV-1 infection	human(IgG1κ)

Ab type: cluster II **References:** [Binley (1996)]

- Fab T3: Binds to cluster II region – competes with MAbs 126-6, Md-1 and D50 – conformation sensitive – variable regions sequenced [Binley (1996)]

803	Md-1 (MD-1)	Env(dis)	gp41(dis)	no		human(IgG1λ)

Ab type: cluster II **Donor:** R. A. Myers State of Maryland Dept. of Health
References: [Myers (1993), Chen (1995), Binley (1996)]

- Md-1: Called MD-1 – discontinuous epitope that binds in the N-terminal region – reacts exclusively with oligomer [Myers (1993)]
- Md-1: Called MD-1 – one of several anti-gp41 MAbs that bind to a gp41-maltose binding fusion protein designed to study the leucine zipper domain of gp41, showing that the construct has retained aspects of normal gp41 conformation [Chen (1995)]
- Md-1: Discontinuous epitope recognizing residues between 563–672, does not recognize cluster I disulfide bridge region – reacts almost exclusively with trimers and tetramers on WB – designated cluster II – Fabs D5, D11, G1, T3, M12, M15, S6, S8, S9, S10 block binding [Binley (1996)]
- Md-1: NIH AIDS Research and Reference Reagent Program: 1223

804 Fab A9 Env(dis) gp41(dis LAI) no HIV-1 infection human(IgG1κ)
Ab type: cluster III **References:** [Binley (1996)]
- Fab A9: Binds to cluster III region – competes with MAb Md-1, but not MAbs 126-6 and D50 – conformation sensitive – variable regions sequenced [Binley (1996)]

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805 Fab G15 Env(dis) gp41(dis LAI) no HIV-1 infection human(IgG1κ)
Ab type: cluster III **References:** [Binley (1996)]
- Fab G15: Binds to cluster III region – competes with MAb Md-1, but not MAbs 126-6 and D50 – conformation sensitive – variable regions sequenced [Binley (1996)]

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806 Fab G5 Env(dis) gp41(dis LAI) no HIV-1 infection human(IgG1κ)
Ab type: cluster III **References:** [Binley (1996)]
- Fab G5: Binds to cluster III region – competes with MAb Md-1, but not MAbs 126-6 and D50 – conformation sensitive – variable regions sequenced [Binley (1996)]

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807 Fab L1 Env(dis) gp41(dis LAI) no HIV-1 infection human(IgG1κ)
Ab type: cluster III **References:** [Binley (1996)]
- Fab L1: Binds to cluster III region – competes with MAb Md-1, but not MAbs 126-6 and D50 – conformation sensitive – variable regions sequenced [Binley (1996)]

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808 Fab L11 Env(dis) gp41(dis LAI) no HIV-1 infection human(IgG1κ)
Ab type: cluster III **References:** [Binley (1996)]
- Fab L11: Binds to cluster III region – competes with MAb Md-1, but not MAbs 126-6 and D50 – conformation sensitive – variable regions sequenced [Binley (1996)]

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809 Fab L2 Env(dis) gp41(dis LAI) no HIV-1 infection human(IgG1κ)
Ab type: cluster III **Donor:** P. Perrin and D. Burton (Scripps Research Institute, La Jolla, California
References: [Binley (1996), Earl (1997)]
- Fab L2: Binds to cluster III region – competes with MAb Md-1, but not MAbs 126-6 and D50 – conformation sensitive – variable regions sequenced [Binley (1996)]

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810 Chessie 8 Env( ) gp41( ) murine(IgG)
Ab type: cytoplasmic domain **Donor:** G. Lewis
References: [Lewis (1991), Poumbourios (1995), Rovinski (1995)]
- Chessie 8: Used to precipitate gp160 in immunoblots in a study examining the feasibility of using unprocessed gp160 glycoprotein as an immunogen [Rovinski (1995)]

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811 T22 Env(dis) gp120(dis IIIB) Vaccine murine(IgG)
Vaccine: *Vector/type:* vaccinia *Strain:* IIIB *HIV component:* oligomeric gp140
Ab type: Env oligomer **Donor:** P. Earl, National Institute of Allergy and Infectious Diseases, NIH, Bethesda, MD

References: [Earl (1994), Otteken (1996), Sugiura (1999)]

- T22: Pulse label experiments of 4 MAbs (D20, D27, T20, and T22) binding to noncleavable gp140 revealed that these anti-CD4BS MAbs bound with a delay, and that the epitope formed with a $t_{1/2}$ of about 10 minutes [Otteken (1996)]
- T22: A comparison of 25 gp120 specific, conformation dependent MAbs was done – T22 is part of a group of MAbs labeled AII – all AII MAbs were broadly cross-reactive with gp160 from B-clade R5, X4, and R5X4 viruses, and could only partially block CD4 binding [Sugiura (1999)]

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812 8F101 Env(dis) gp120(dis) Vaccine murine(IgG)

Vaccine: *Vector/type:* sCD4-gp120 complex *Strain:* HXB2 *HIV component:* gp120

Ab type: gp120-CD4 complex **References:** [DeVico (1995)]

- 8F101: MAbs specifically reactive to crosslinked gp120 and CD4 were derived (8F101, 8F102) – conformation dependent – competition studies indicate the epitope is immunogenic in infected humans [DeVico (1995)]

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813 8F102 Env(dis) gp120(dis) Vaccine murine(IgG)

Vaccine: *Vector/type:* sCD4-gp120 complex *Strain:* HXB2 *HIV component:* gp120

Ab type: gp120-CD4 complex **References:** [DeVico (1995)]

- 8F102: MAbs specifically reactive to crosslinked gp120 and CD4 were derived (8F101, 8F102) – conformation dependent – competition studies indicate the epitope is immunogenic in infected humans [DeVico (1995)]

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814 CG-10 (CG10) Env(dis) gp120(dis IIIB) L Vaccine murine(IgG1)

Vaccine: *Vector/type:* sCD4-gp120 complex *Strain:* IIIB *HIV component:* gp120

Ab type: gp120-CD4 complex **Donor:** Jonathan Gershoni, Tel Aviv University, Isreal
References: [Gershoni (1993), Wu (1996), Lee (1997), Rizzuto (1998), Sullivan (1998b), Oscherwitz (1999)]

- CG-10: Reacts exclusively with sCD4-gp120 complex, not with sCD4 or gp120 alone [Gershoni (1993)]
- CG-10: Called CG10 – MIP-1α binding to CCR-5 expressing cells can be inhibited by gp120-sCD4, and MAb CG10 does not block this inhibition [Wu (1996)]
- CG-10: Called CG10 – Promotes envelope mediated cell fusion between CD4+ cells and cells infected with either T-cell and macrophage tropic viruses – infection of HeLa CD4+ (MAGI) cells by HIV-1 LAI, ELI1, and ELI2 strains was increased two-to four-fold in the presence of CG10 [Lee (1997)]
- CG-10: Called CG10 – disrupts gp120-CCR5 interaction and competes with MAb 17b –binds near the conserved bridging sheet of gp120 – mutations in positions K/D 121, T/D 123, K/D 207, K/D 421, Q/L 422, Y/S 435, M/A 434, K/A 432 and I/S 423 result in a 70% reduction in CG10 binding [Rizzuto (1998)]

- CG-10: Called CG10 – CD4BS MAb 15e competes with CG-10 binding, probably due to the disruption of CD4-gp120 by 15e – CD4i MAbs 17b and 48d compete and the binding sites may overlap – MAb A32 enhances binding of 17b, 48d and CG10 – MAbs C11, 2G12 and 212A do not affect CG10 binding – CG-10 can bind gp120 with V1/V2 and V3 deleted – HXBc2 mutations Δ 119–205, 314 G/W, 432 K/A, 183,184 PI/SG decrease CG-10 recognition, HXBc2 mutations Δ 298–327 (V3), 384 Y/E, 298 R/G, 435 Y/S enhance recognition – the CD4 contribution to the CG10 epitope maps to the CD4 CDR2-like loop – CG10 can neutralize HIV-1 in the presence of sCD4 even though it does not do so in the context of cell surface CD4 binding to gp120 [Sullivan (1998b)]

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815 CG-25 Env(dis) gp120(dis) L Vaccine murine(IgG1)

Vaccine: *Vector/type:* sCD4-gp120 complex *HIV component:* gp120

Ab type: gp120-CD4 complex **References:** [Gershoni (1993)]

- CG-25: Reacts preferentially with sCD4-gp120, also with sCD4, not with gp120 [Gershoni (1993)]

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816 CG-4 (CG4) Env(dis) gp120(dis) no Vaccine murine(IgG1)

Vaccine: *Vector/type:* sCD4-gp120 complex *HIV component:* gp120

Ab type: gp120-CD4 complex **Donor:** Jonathan Gershoni, Tel Aviv University, Isreal
References: [Gershoni (1993)]

- CG-4: Reacts with gp120 and sCD4-gp120 complex, not with sCD4 [Gershoni (1993)]

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817 CG-76 Env(dis) gp120(dis) L Vaccine murine(IgG1)

Vaccine: *Vector/type:* sCD4-gp120 complex *HIV component:* gp120

Ab type: gp120-CD4 complex **References:** [Gershoni (1993)]

- CG-76: Reacts equally well with sCD4-gp120 and sCD4, but not with purified gp120 [Gershoni (1993)]

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818 CG-9 Env(dis) gp120(dis) L Vaccine murine(IgG1)

Vaccine: *Vector/type:* sCD4-gp120 complex *HIV component:* gp120

Ab type: gp120-CD4 complex **References:** [Gershoni (1993)]

- CG-9: Reacts preferentially with sCD4-gp120, also with sCD4, not with gp120 [Gershoni (1993)]

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819 NC-1 Env(dis) gp41(dis IIIB) Vaccine murine(IgG2a)

Vaccine: *Vector/type:* peptide *Strain:* IIIB *HIV component:* a peptide that folds into a six helix bundle like gp41

Ab type: helical core **Donor:** S. Jiang, New York Blood Center, NY, NY
References: [Jiang (1998)]

- NC-1: Ab elicited in response to immunization with N36(L6)C34, a peptide that folds into a six helix bundle like gp41 – NC-1 binds to the surface of HIV-1 infected cells only in the presence of sCD4, recognizing the fusogenic core structure – binding affinity was decreased by point mutations that disrupt core formation and abolish membrane fusion activity, (I573P and I573A) – NC-1 can recognize discontinuous epitopes from B clade isolate SC, but not E clade strain N243, O group strain GAB, or HIV-2 ROD [Jiang (1998)]

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820 105–518 Env( ) gp41(608–637 HAM112, O group) Vaccine murine(IgG1κ)

Vaccine: *Vector/type:* recombinant protein *Strain:* HAM112 (group O) *HIV component:* gp160

Ab type: immunodominant region **References:** [Scheffel (1999)]

- 101–518: Overlapping peptides based on group O HAM112 Env were tested for MAb reactivity [Scheffel (1999)]

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821 2A2 Env( ) gp41( ) no HIV-1 infection human(IgG1κ)

Ab type: N-term **References:** [Weissenhorn (1996)]

- Soluble gp41(21–166) forms a rod like structure that can be visualized with electron microscopy, and 2A2 binds to one end of the rod [Weissenhorn (1996)]

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822 AC4 Env(dis 1–204) gp120(dis IIIB) yes Vaccine murine( )

Vaccine: *Vector/type:* recombinant protein *HIV component:* gp160

Ab type: N-term **References:** [Dickey (2000)]

- AC4: Three MABs, ID6, AC4, and AD3 that bind to a discontinuous N-term first 204 aa of gp120 and generate ADCC were elicited through vaccination of BALBc mice with rec gp160 – these MAbs do not depend on glycosylation and are cross-reactive with viruses from clades B and CRF01(AE) [Dickey (2000)]

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823 AD3 Env(dis 1–204) gp120(dis IIIB) yes Vaccine murine( )

Vaccine: *Vector/type:* recombinant protein *HIV component:* gp160

Ab type: N-term **References:** [Dickey (2000)]

- AD3: There may be two Abs with this name that bind to the N-term region of gp120 [Cook (1994), Dickey (2000)]
- AD3: Three MABs, ID6, AC4, and AD3 that bind to a discontinuous N-term first 204 aa of gp120 and generate ADCC were elicited through vaccination of BALBc mice with rec gp160 – these MAbs do not depend on glycosylation and are cross-reactive with viruses from clades B and CRF01(AE) [Dickey (2000)]

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824 AD3 Env(dis 1–193) gp120(dis BH10) murine(IgG1)

Ab type: N-term **References:** [Ugen (1993), Cook (1994)]

- AD3: There may be two Abs with this name that bind to the N-term region of gp120 [Cook (1994), Dickey (2000)]
- AD3: MAbs against the glycosphingolipid GalCer block HIV infection of normally susceptible CD4 negative cells from the brain and colon – MAbs against the N-terminal half of gp120 do not inhibit gp120 binding to GalCer – binding of GalCer to gp120 does not inhibit MAb binding [Cook (1994)]
- AD3: NIH AIDS Research and Reference Reagent Program: 2342

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825 ID6 Env( ) gp120(1–193 BH10) ined amino terminus murine(IgG1)

Ab type: N-term **References:** [Ugen (1993), Cook (1994)]

- ID6: There may be two Abs with this name that bind to the N-term region of gp120 [Cook (1994), Dickey (2000)]
- ID6: MAbs against the glycosphingolipid GalCer block HIV infection of normally susceptible CD4 negative cells from the brain and colon – MAbs against the N-terminal half of gp120 do not inhibit gp120 binding to GalCer – binding of GalCer to gp120 does not inhibit MAb binding [Cook (1994)]

- ID6: NIH AIDS Research and Reference Reagent Program: 2343

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826 ID6 Env(dis 1–204) gp120(dis IIIB) yes Vaccine murine(IgG2a)

Vaccine: *Vector/type:* recombinant protein *HIV component:* gp160

Ab type: N-term **References:** [Dickey (2000)]

- ID6: There may be two Abs with this name that bind to the N-term region of gp120 [Cook (1994), Dickey (2000)]
- ID6: Three MABs, ID6, AC4, and AD3 that bind to a discontinuous N-term first 204 aa of gp120 and generate ADCC were elicited through vaccination of BALBc mice with rec gp160 – these MAbs do not depend on glycosylation and are cross-reactive with viruses from clades B and CRF01(AE) [Dickey (2000)]

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827 31A1 Env( ) gp41( ) no *in vitro* stimulation human(IgMκ/λ)

Ab type: p24+gp41 **References:** [Pollock (1989)]

- 31A1: Denatured virus was used for *in vitro* stimulation to generate Abs – Reacts with both p24 and gp41 [Pollock (1989)]

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828 39A64 Env( ) gp41( ) no *in vitro* stimulation human(IgMκ/λ)

Ab type: p24+gp41 **References:** [Pollock (1989)]

- 39A64: Denatured virus was used for *in vitro* stimulation to generate Abs – Reacts with both p24 and gp41 [Pollock (1989)]

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829 39B86 Env( ) gp41( ) no *in vitro* stimulation human(IgMκ/λ)

Ab type: p24+gp41 **References:** [Pollock (1989)]

- 39B86: Denatured virus was used for *in vitro* stimulation to generate Abs – Reacts with both p24 and gp41 [Pollock (1989)]

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830 9303 Env( ) gp41( ) no murine( )

Ab type: p24+gp41 **Donor:** Du Pont

References: [McDougal (1996)]

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831 polyclonal Env(dis) Env(dis) yes HIV-1 infection human( )

Ab type: V1-V2 and V3-V5 **References:** [Gordon & Delwart(2000)]

- Primary isolates have great differences in susceptibility to neutralization – the variation in V1V2 and V3-V5 was measured by HTA in a set of viruses with a range of neutralization susceptibilities, and greater variability was uncorrelated with resistance to neutralization [Gordon & Delwart(2000)]

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832 11/68b Env(dis) gp120(dis) L (HXB2) Vaccine rat(IgG1)

Vaccine: *Vector/type:* recombinant protein *Strain:* BH10 *HIV component:* gp120

Ab type: V1V2 **Donor:** Shotton and Dean

References: [McKeating (1993b), Shotton (1995), Peet (1998)]

- 11/68b: Changes at residues 183/184 (PI/SG) within V2, 435 (Y/H) in C4, abrogate binding [McKeating (1993b)]
- 11/68b: 435 (Y/H) in C4 does not abrogate binding (John Moore, per comm, 1996)
- 11/68b: Cross-competes with MAbs 62c, 66c, 66a, and CRA-4 – similar to MAb 62c – HXB2 neutralization escape mutant had a D/N substitution at residue 185 – non-reciprocal inhibition of binding of CRA-3 and CRA-6 [Shotton (1995)]

- 11/68b: The most variable amino acids in the V3 loop were replaced with serines to make the immunodominant V3 loop less immunogenic – these changes did not affect the ability of sCD4 or MAbs to V1/V2, C1 and C4 to bind – 11/68b was not affected by V3 serine substitutions – mice injected with serine substituted gp120 had a reduced response relative to wildtype, and no enhanced immunogenicity of conserved regions [Peet (1998)]
- 11/68b: UK Medical Research Council AIDS reagent: ARP3041

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833 62c Env(dis) gp120(dis) no Vaccine rat(IgG1)

Vaccine: *Vector/type:* recombinant protein *Strain:* BH10 *HIV component:* gp120

Ab type: V1V2 **References:** [Shotton (1995)]

- 62c: Cross-competes with MAbs 11/68b, 66c, 66a, and CRA-4 – same cross-competition group as MAb 11/68b – non-reciprocal inhibition of binding of CRA-3 and CRA-6 – substitutions 176–177 FY/AT, 179–180 LD/DL, 183–184 PI/SG, and 191–193 YSL/GSS abrogate binding – binds but does not neutralize Hx10 [Shotton (1995)]
- 62c: UK Medical Research Council AIDS reagent: ARP3075

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834 CRA-6 (CRA6) Env(dis) gp120(dis) no murine( )

Ab type: V1V2 **References:** [Shotton (1995)]

- CRA-6: Called CRA6 – same competition group as CRA-3 [Shotton (1995)]

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835 L15 Env(dis) gp120(dis) P (weak) HIV-1 infection human(IgG1)

Ab type: V1V2 **References:** [Ditzel (1997), Parren (1997b)]

- L15: gp120 immobilized on solid phase by capture with anti-CD4 BS MAb L72 was used for selection of Fabs – 2 anti-V2 Fabs were obtained with very similar epitopes, L15 and L17 – deletions in V1 and V2 abolished binding, and rodent anti-V2 MAbs SC258, CRA3, G3-G4,G3-136, BAT-085, and 52–684 all compete with L15 [Ditzel (1997)]
- L15: Does not neutralize TCLA strains but neutralizes some primary isolates weakly [Parren (1997b)]

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836 T52 Env(dis) gp120(dis IIIB) Vaccine murine(IgG)

Vaccine: *Vector/type:* vaccinia *Strain:* IIIB *HIV component:* oligomeric gp140

Ab type: V1V2 **Donor:** P. Earl, National Institute of Allergy and Infectious Diseases, NIH, Bethesda, MD
References: [Earl (1994), Sugiura (1999)]

- T52: A comparison of 25 gp120 specific, conformation dependent MAbs was done – T52 is one of two MAbs labeled B-II, that had limited cross-reactivity with seven clade B isolates and did not fully blocked CD4 binding – deletion of V1/V2 loops abrogated binding [Sugiura (1999)]

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837 T54 Env(dis) gp120(dis IIIB) no Vaccine murine(IgG)

Vaccine: *Vector/type:* vaccinia *Strain:* IIIB *HIV component:* oligomeric gp140

Ab type: V1V2 **Donor:** P. Earl, National Institute of Allergy and Infectious Diseases, NIH, Bethesda, MD
References: [Earl (1994), Sugiura (1999)]

- T54: A comparison of 25 gp120 specific, conformation dependent MAbs was done – T54 is one of two MAbs labeled B-II, that had limited cross-reactivity with seven clade B isolates and did not fully blocked CD4 binding – deletion of V1/V2 loops abrogated binding [Sugiura (1999)]

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838 1088 Env( ) gp120( ) ( )
Ab type: V2 **References:** [Berman (1997)]
- 1088: Binds weakly to 2/7 isolates from breakthrough cases from a MN gp120 vaccine trial [Berman (1997)]

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839 110-B Env(dis) gp120(dis) no Vaccine murine( )
Vaccine: *Vector/type:* infected-cell lysate *Strain:* BRU *HIV component:* virus
Ab type: V2 **Donor:** Hybridolabs, Institute Pasteur, Paris, France
References: [Moore (1993a)]
- 110-B: specific for BH10, does not bind to MN, RF, or SF-2 gp120 – binding inhibited by deletion of the V2 loop, and the following amino acid substitutions: 168 K/L, 176/177 FY/AT, 179/180 LD/DL, 183/184 PI/SG, and 192–194 YSL/GSS [Moore (1993a)]

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840 1357 Env( ) gp120( ) human(IgG1κ)
Ab type: V2 **Donor:** Susan Zolla-Pazner (Zollas01@mcrcr6.med.nyu) (NYU Med. Center)
References: [Nyambi (1998), Gorny (2000), Nyambi (2000)]
- 1357: 26 HIV-1 group M isolates (clades A to H) were tested for binding to 47 MAbs, including 5 anti-V2 MAbs, which showed weak and sporadic binding, with the most frequent binding to C and D clades [Nyambi (2000)]
- 1357: Using a whole virion-ELISA method, 18 human MAbs were tested for their ability to bind to a panel of 9 viruses from clades A, B, D, F, G, and H – V2 Abs 697-D, 1361, and 1357 tended to bind very weakly with a similar pattern of specificity to virions, but bound well to soluble gp120: weak binding only to subtype D MAL [Nyambi (1998)]
- 1357: Blocks binding of MAb 697-D to rgp120, and doesn't react with a protein from which V1V2 has been deleted – binding of panel of 21 MAbs to soluble oligomeric gp140 versus gp41 or gp120 monomers was compared – no MAb was oligomer specific, though anti-V3 and CD4BS MAbs reacted better with the oligomer and V2 and C5 tended to favor the monomer – V2 MAbs 697-D, 1357 and 1361 favored the monomer by approximately 2 fold [Gorny (2000)]
- 1357: 26 HIV-1 group M isolates (clades A to H) were tested for binding to 47 MAbs, including 5 anti-V2 MAbs, which showed weak and sporadic binding, with the most frequent binding to C and D clades [Nyambi (2000)]

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841 1361 Env( ) gp120( ) Vaccine human(IgG1κ)
Vaccine: *Vector/type:* protein *HIV component:* gp120
Ab type: V2 **Donor:** Susan Zolla-Pazner (Zollas01@mcrcr6.med.nyu) (NYU Med. Center)
References: [Nyambi (1998), Gorny (2000), Nyambi (2000)]
- 1361: Using a whole virion-ELISA method, 18 human MAbs were tested for their ability to bind to a panel of 9 viruses from clades A, B, D, F, G, and H – V2 Abs 697-D, 1361, and 1357 tended to bind weakly with a similar pattern of specificity to virions, but bound well to soluble gp120: weak binding to 1/4 B clade viruses (CA5), and also weak binding to a subtype D virus, MAL [Nyambi (1998)]

- 1361: Blocks binding of MAb 697-D to rgp120, and doesn‘t react with a protein from which V1V2 has been deleted – binding of panel of 21 MAbs to soluble oligomeric gp140 versus gp41 or gp120 monomers was compared – no MAb was oligomer specific, though anti-V3 and CD4BS MAbs reacted better with the oligomer and V2 and C5 tended to favor the monomer – V2 MAbs 697-D, 1357 and 1361 favored the monomer by approximately 2 fold [Gorny (2000)]
- 1361: 26 HIV-1 group M isolates (clades A to H) were tested for binding to 47 MAbs, including 5 anti-V2 MAbs, which showed weak and sporadic binding, with the most frequent binding to C and D clades [Nyambi (2000)]

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842 1393A Env( ) gp120( ) HIV-1 infection ( )

Ab type: V2 **References:** [Nyambi (2000)]

- 1393A: 26 HIV-1 group M isolates (clades A to H) were tested for binding to 47 MAbs, including 5 anti-V2 MAbs, which showed weak and sporadic binding, with the most frequent binding to C and D clades [Nyambi (2000)]

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843 66a Env(dis) gp120(dis) L (HXB2) Vaccine murine(IgG1)

Vaccine: *Vector/type:* recombinant protein *Strain:* BH10 *HIV component:* gp120

Ab type: V2 **References:** [Shotton (1995)]

- 66a: Substitutions 176–177 FY/AT, 179–180 LD/DL, 183–184 PI/SG, and 191–193 YSL/GSS abrogate binding – same competition group as CRA4 [Shotton (1995)]
- 66a: UK Medical Research Council AIDS reagent: ARP3074

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844 66c Env(dis) gp120(dis) L (HXB2) Vaccine murine(IgG1)

Vaccine: *Vector/type:* recombinant protein *Strain:* BH10 *HIV component:* gp120

Ab type: V2 **References:** [Shotton (1995)]

- 66c: Substitutions 176–177 FY/AT, 179–180 LD/DL, 183–184 PI/SG, and 191–193 YSL/GSS abrogate binding – same competition group as CRA4 [Shotton (1995)]

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845 684–238 (52–684-238, 52–684) Env(dis) gp120(dis) L Vaccine murine( )

Vaccine: *Vector/type:* purified protein *Strain:* IIIB *HIV component:* gp120

Ab type: V2 **Donor:** Gerry Robey, Abbott Laboratories
References: [Moore (1993a), Thali (1993), Gorny (1994), Ditzel (1995), Moore & Sodroski(1996), Ditzel (1997)]

- 684–238: Specific for BH10 or HXB2, does not bind to MN, RF, or SF-2 gp120 – neutralizes BH10 – binding inhibited by deletion of the V2 loop, and the following amino acid substitutions: 176/177FY/AT, 179/180LD/DL, 183/184PI/SG, and 192–194YSL/GSS [Moore (1993a)]
- 684–238: Weakly neutralizing, IC 50 = 84 μg/ml [Gorny (1994)]
- 684–238: Does not compete with IgG1b12, reciprocal inhibition with MAbs L39, L40, and L78 [Ditzel (1995)]
- 684–238: Limited reciprocal enhancement of binding with anti-V3 and C4 region antibodies – reciprocal inhibition with V2 region antibodies [Moore & Sodroski(1996)]

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846 830A Env( ) gp120( ) HIV-1 infection ( )

Ab type: V2 **References:** [Nyambi (2000)]

- 830A: 26 HIV-1 group M isolates (clades A to H) were tested for binding to 47 MAbs, including 5 anti-V2 MAbs, which showed weak and sporadic binding, with the most frequent binding to C and D clades [Nyambi (2000)]

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847 CRA-3 (CRA3) Env(dis) gp120(dis) no Vaccine murine(IgG2a)

Vaccine: *Vector/type:* recombinant protein *Strain:* BH10 *HIV component:* gp120

Ab type: V2 **Donor:** Mark Page, NIBSC AIDS reagent project, Potters Bar, Herts, UK

References: [Moore & Ho(1993), Moore (1993a), Thali (1993), Shotton (1995), Moore & Sodroski(1996), Ditzel (1997)]

- CRA-3: Conformational, does not bind well to denatured gp120 [Moore & Ho(1993)]
- CRA-3: specific for BH10 or HXB2, does not bind to MN, RF, or SF-2 gp120 – binding inhibited by deletion of the V2 loop, and the following amino acid substitutions: 176/177 FY/AT, 179/180 LD/DL, 183/184 PI/SG, and 192–194 YSL/GSS – epitope probably involves stem of V1/V2 loop structure [Moore (1993a)]
- CRA-3: Many MAbs enhance binding, including some anti-C5, C1, V4, and C4 MAbs – enhances binding of only a small number of anti-V3 loop MAbs [Moore & Sodroski(1996)]
- CRA-3: Called CRA3 – Same competition group as CRA6 [Shotton (1995)]
- CRA-3: UK Medical Research Council AIDS reagent: ARP324

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848 CRA-4 (CRA4) Env(dis) gp120(dis) L (HXB2) Vaccine murine(IgG1)

Vaccine: *Vector/type:* recombinant protein *Strain:* BH10 *HIV component:* gp120

Ab type: V2 **Donor:** Mark Page, NIBS, MRC AIDS reagent repository, ARP 325

References: [McKeating (1993b), Moore & Ho(1993), Moore (1993a), Thali (1993), Shotton (1995), Moore & Sodroski(1996)]

- CRA-4: Changes at residues 191/192/193 (YSL/GSS) within V2, 435 (Y/H) in C4, abrogate binding – type-specific neutralization [McKeating (1993b)]
- CRA-4: Conformational, does not bind well to denatured gp120 [Moore & Ho(1993)]
- CRA-4: Specific for BH10 and HXB2, does not bind to MN, RF, or SF-2 gp120 – binding inhibited by deletion of the V2 loop, and the following amino acid substitutions: 176/177 FY/AT, 179/180 LD/DL, 183/184 PI/SG, and 192–194 YSL/GSS [Moore (1993a)]
- CRA-4: Cross-competes with MAbs 11/68b, 62c, 66c, 66a – similar to 66c and 66a – non-reciprocal inhibition by MAbs 12b, 60b and CRA-6 [Shotton (1995)]
- CRA-4: The only MAbs that enhanced binding were anti-V3 MAb 5G11 and anti-C1 MAb 135/9 binding – reciprocal inhibition of anti-V2 MAbs [Moore & Sodroski(1996)]
- CRA-4: UK Medical Research Council AIDS reagent: ARP325

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849 L17 Env(dis) gp120(dis) human Fab( )

Ab type: V2 **References:** [Ditzel (1997), Parren (1998a)]

- L17: The rank order of Fab binding affinity to monomeric gp120 (Loop 2 > 3B3 > b12 = DO8i > b11 > b3 > b14 > b13 > DO142–10 > DA48 > L17) was markedly different than Fab binding affinity to the mature oligomeric form (3B3 > b12 > DO142–10 > Loop 2 > b11 > L17 > b6 > DO8i > b14 > DA48 > b3 > b13) and binding to oligomeric form and neutralization were correlated for both Fabs and MAbs – authors suggest that neutralization is determined by the fraction of Ab sites occupied on a virion irrespective of the epitope [Parren (1998a)]

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850 SC258 (52–581-SC258) Env(dis) gp120(dis) L Vaccine murine( )

Vaccine: *Vector/type:* purified protein *Strain:* IIIB *HIV component:* gp120

Ab type: V2 **Donor:** Gerry Robey, Abbott Laboratories

References: [Moore (1993a), Thali (1993), Gorny (1994), Yoshiyama (1994), Moore (1994b), Ditzel (1995), Moore & Sodroski(1996), Trkola (1996a), Ditzel (1997)]

- SC258: Called 52–581-SC258 – binds to BH10, MN, and RF gp120 – neutralizes BH10 – binding inhibited by deletion of the V2 loop, and the following amino acid substitutions: 176/177 FY/AT, 179/180 LD/DL, 183/184 PI/SG, and 192–194 YSL/GSS [Moore (1993a)]
- SC258: HIV-1 RF V2 substitutions 177 Y/H and 179 L/P in the V2 loop of RF reduce affinity – 177 Y/H inhibits SC258 neutralization [Yoshiyama (1994)]
- SC258: Very poor reactivity with gp120 molecules outside of clade B [Moore (1994b)]
- SC258: Does not compete with IgG1b12 – reciprocal inhibition with MAbs L39, L40, and L78 [Ditzel (1995)]
- SC258: Several MAbs binding to various gp120 epitopes enhance binding, but the only MAb that SC258 enhanced binding of was anti-CD4 binding site MAb F91 – reciprocal inhibition with V2 region antibodies [Moore & Sodroski(1996)]
- SC258: Does not inhibit gp120 interaction with CCR-5 in a MIP-1β-CCR-5 competition study – listed as not neutralizing [Trkola (1996a)]

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851 L25 Env(dis) gp120(dis) L (weak) HIV-1 infection human(IgG1)

Ab type: V2-CD4BS **References:** [Ditzel (1995), Ditzel (1997), Parren (1997b)]

- L25: gp120 immobilized on solid phase by capture with anti-CD4 BS MAb L72 was used for selection of Fabs – a single anti-V2-CD4 BS Fab was obtained with with sensitivity to substitutions in the V2 and CD4 BS regions – rodent anti-V2 MAb SC258 competes with L25 [Ditzel (1997)]
- L25: Neutralizes TCLA strains weakly, but not primary isolates [Parren (1997b)]

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852 L39 Env(dis) gp120(dis) no HIV-1 infection human(IgG1κ)

Ab type: V2-CD4BS **References:** [Ditzel (1995)]

- L39: This Fab does not inhibit sCD4 binding, but is inhibited by sCD4, probably due to conformational changes – it is competed by anti-V2 MAbs, and sensitive to amino acid substitutions in the V3 loop (similar patterns were observed for L39 and L78 gp120 amino acid substitutions enhancing or reducing binding) – does not compete with CD4BS MAbs, but is sensitive to amino acid changes at positions 368 and 370 – binding unaffected by deglycosylation – reciprocal inhibition with V2 MAbs SC258 and 684–238 – heavy and light chain variable region sequence is available [Ditzel (1995)]

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853 L40 Env(dis) gp120(dis) no HIV-1 infection human(IgG1κ)

Ab type: V2-CD4BS **References:** [Ditzel (1995)]

- L40: This Fab does not inhibit sCD4 binding, but is inhibited by sCD4, probably due to conformational changes – it is competed by anti-V2 MAbs, and sensitive to amino acid substitutions in the V3 loop (similar patterns were observed for L40 and L78 gp120 amino acid substitutions enhancing or reducing binding) – does not compete with CD4BS MAbs, but is sensitive to amino acid changes at positions 368 and 370 – binding only partially affected by deglycosylation – reciprocal inhibition with V2 MAbs SC258 and 684–238 – heavy and light chain variable region sequence is available [Ditzel (1995)]

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854 L78 Env(dis) gp120(dis) L HIV-1 infection human(IgG1κ)

Ab type: V2-CD4BS **References:** [Ditzel (1995)]

- L78: Substitutions at V2: (152/153 GE/SM, 183/184 PI/SG, 191/193 YL/GS), 262 N/T, V3 (314 G/W), CD4BS (257 T/R, 368 D/R, 370 E/R) inhibit binding, and some C4 and C5 substitutions enhance binding – this Fab does not inhibit sCD4 binding, but is inhibited by sCD4, probably due to conformational changes – it is competed by anti-V2 MAbs, and sensitive to amino acid substitutions in the V3 loop – does not compete with CD4BS MAbs, but is sensitive to amino acid changes at positions 368 and 370 – Fab neutralizes MN and LAI – binding unaffected by deglycosylation – reciprocal inhibition with V2 MAbs SC258 and 684–238 – heavy and light chain variable region sequence is available [Ditzel (1995)]

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855 110.J Env( ) gp120( ) ( )

Ab type: V3 **Donor:** F. Traincard, Pasteur Institute, France

References: [Thali (1993), Moore & Sodroski(1996)]

- 110.J: Inhibits sCD4-inducible anti-CD4 binding site MAb 48d [Thali (1993)]
- 110.J: Binds to carboxy-terminal side of the V3 loop – reciprocal binding inhibition with other anti-V3 and anti-C4 MAbs – and reciprocal enhanced binding of some anti-V2 MAbs and anti-CD4 binding site MAbs [Moore & Sodroski(1996)]

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856 1334-D (1334, 1334D) Env( ) gp120(HIV451) HIV-1 infection human(IgG1κ)

Ab type: V3 **Donor:** Susan Zolla-Pazner (Zollas01@mcrcr6.med.nyu) (NYU Med. Center)

References: [Zolla-Pazner (1999a), Zolla-Pazner (1999b), Gorny (2000)]

- 1334-D: This MAb was selected on oligomeric gp160 from HIV451 [Zolla-Pazner (1999a)]
- 1334-D: MAb peptide-reactivity pattern clustered with immunological related MAbs: 1334, 419, 504, 447, 453 and 537 – the core amino acids GP tended to be critical for reactivity in this group [Zolla-Pazner (1999b)]

- 1334-D: Called 1334 – binds to V3 peptides from MN, SF2, NY5, RF, and CDC4 strains as well as x-reactivity with peptides from A, C, D, F, G, and H subtypes – was suggested to be IgG1lambda here – binding of panel of 21 MAbs to soluble oligomeric gp140 versus gp41 or gp120 monomers was compared – no MAb was oligomer specific, though anti-V3 and CD4BS MAbs reacted better with the oligomer and V2 and C5 tended to favor the monomer – V3 MAbs 447-52D, 838-D, and 1334 bound with a 7–10 fold preference for the oligomer [Gorny (2000)]
- 1334-D: Called 1334D – A panel of 47 human MAbs was tested against 26 HIV-1 group M primary isolates from clades A through H – 19 V3 MABs were tested, and of 494 combinations, 44% displayed some viral binding – V3 MAbs tended to have the most cross-reactive binding to clade A, B, C, and D isolates, less to E, F, G, and H – 1334D showed intermediate cross-reactivity [Nyambi (2000)]

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857 55/68b Env( ) gp120(300–315) ( )

Ab type: V3 **References:** [Peet (1998)]

- 55/68b: The most variable amino acids in the V3 loop were replaced with serines to make the immunodominant V3 loop less immunogenic – these changes did not affect the ability of sCD4 or MAbs to V1/V2, C1 and C4 to bind, and anti-V3 MAb 55/68b binding was abrogated by V3 serine substitutions in the V3 loop – mice injected with serine substituted gp120 had a reduced response relative to wildtype, and no enhanced immunogenicity of conserved regions [Peet (1998)]

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858 5G11 Env( ) gp120( ) ( )

Ab type: V3 **Donor:** S. Nigida and L. Arthur, NCI, Frederick, MD USA

References: [Moore & Sodroski(1996)]

- 5G11: Binds to conformation sensitive epitope in the V3 loop – reciprocal inhibition of other V3 loop MAbs – reciprocal enhancement of some C1-C5 MAbs (unusual for an anti-V3 MAb) and CD4 binding site MAbs – and enhances binding of V2 MAbs [Moore & Sodroski(1996)]

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859 9305 Env( ) gp120( ) L murine( )

Ab type: V3 **Donor:** Du Pont, Wilmington DE

References: [McDougal (1996)]

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860 AG1121 (1121) Env( ) gp120( ) L ( )

Ab type: V3 **Donor:** AGMED, Inc, Bedford MA, commercial

References: [Sullivan (1995), Cao (1997)]

- AG1121: Recognizes monomeric gp120 from T-cell adapted line HXBc2 and primary isolate 89.6 equally well, but 89.6 was three-fold less sensitive to neutralization by AG1121 than HXBc2 [Sullivan (1995)]
- AG1121: Called 1121 – Virus with the V1-V2 loop deleted was viable and more susceptible to neutralization by CD4i MAb 17b, and anti-V3 MAbs 1121, 9284, and 110.4, but not to and CD4BS MAb F105 or sCD4 [Cao (1997)]

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861 anti-gp120/V3 | Env( ) | gp120( ) | Vaccine | murine(IgG)

Vaccine: *Vector/type:* recombinant protein, virus-like particle *Strain:* A clade 94UG018 *HIV component:* Gag, Pol, Nef, gp120

Ab type: V3 **Donor:** Intracel Co
References: [Buonaguro (2001)]

- Anti-V3: HIV-1 pr55 gag-based virus-like particles (VLP) carrying Nef and Pol open reading frames as well as gp120 of the clade A isolate 94UG018 were created using a Baculovirus expression system to package additional ORFS into the VLP – anti-V3 and anti-p24 antibodies were used to assess the expression levels and Gag and gp120-TM were found to be expressed at comparable levels on the VLP

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862 D47 | Env( ) | gp120(IIIB) | Vaccine | murine( )

Vaccine: *Vector/type:* vaccinia *Strain:* IIIB *HIV component:* Env

Ab type: V3 **Donor:** Patricia Earl, NIAID, NIH
References: [Earl (1994), Richardson (1996), Otteken (1996), Wyatt (1997), Earl (1997), Salzwedel (2000)]

- D47: Used for capture of oligomeric Env for antigen capture ELISA – binding of this antibody to oligomeric Env IIIB was not blocked by human sera from the US, consistent with a low prevalence of IIIB-like V3 strains [Richardson (1996)]
- D47: Pulse label experiments of MAb binding to noncleavable gp160 revealed that this anti-V3 MAb bound immediately and binding stayed constant through chase period [Otteken (1996)]
- D47: Binds both gp120 and soluble gp120+gp41 complex efficiently, suggesting its gp120 epitope is not blocked by gp41 binding [Wyatt (1997)]
- D47: Used for comparison in a study of gp41 antibodies – D47 binds to a greater extent to cell surface expressed Env than any of 38 conformation dependent anti-gp41 MAbs [Earl (1997)]
- D47: sCD4 can activate fusion between effector cells expressing Env and target cells expressing coreceptor (CCR5 or CXCR4) alone without CD4 – V3 MAb D47 is strain specific and can inhibit sCD4 mediated infection, but only of the closely related LAV Env, while anti-CD4i MAbs were broadly cross-neutralizing [Salzwedel (2000)]

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863 F5.5 | Env( ) | gp120(IIIB) | murine( )

Ab type: V3 **Donor:** Hybridolabs, Institute Pasteur
References: [Altmeyer (1999)]

- F5.5: A Semliki Forest virus (SFV) expression system carrying BX08 env was used to study the conformation of gp120 Env – intracytoplasmic gp120 was recognized by the anti-V3 MAbs K24 and F5.5, while gp120 at the plasma membrane was detected only by conformation dependent MAbs 2G12, 670-D and 694/98D and not V3 MAbs – expression in rat brain also showed that surface-expressed Env was recognized only by the conformation-dependent antibodies and not by anti-V3 antibodies [Altmeyer (1999)]

864	G3-1472	Env( )	gp120( )			( )

Ab type: V3 **Donor:** M. Fung
References: [Moore & Sodroski(1996)]

- G3-1472: Binds to carboxy-terminal side of the V3 loop – reciprocal binding inhibition with other anti-V3 and anti-C4 MAbs – reciprocal enhanced binding of some anti-V2 MAbs and anti-CD4 binding site MAbs – binding inhibited by anti-C4 MAbs [Moore & Sodroski(1996)]

865	K24	Env( )	gp120(IIIB)			murine( )

Ab type: V3 **Donor:** Hybridolabs, Institute Pasteur
References: [Altmeyer (1999)]

- K24: A Semliki Forest virus (SFV) expression system carrying BX08 env was used to study the conformation of gp120 env – intracytoplasmic gp120 was recognized by the anti-V3 MAbs K24 and F5.5, while gp120 at the plasma membrane was detected only by conformation dependent MAbs 2G12, 670-D and 694/98D and not V3 MAbs – expression in rat brain also showed that surface-expressed Env was recognized only by the conformation-dependent antibodies and not by anti-V3 antibodies [Altmeyer (1999)]

866	M096/V3	Env(dis 309–318 + 329–338)	gp120(dis 309–318)	IQRGPGRAFV + AHCNISRAKW	*in vitro* stimulation	human(IgM)

Ab type: V3 **References:** [Ohlin (1992)]

- M096: Generated in response to IIIB Env 286–467 upon *in vitro* stimulation of uninfected-donor lymphocytes, and binds to two peptides: 309–318 + 329–338 [Ohlin (1992)]

867	polyclonal	Env( )	gp120( )	yes	Vaccine	human( )

Vaccine: *Vector/type:* canarypox prime with recombinant protein boost *Strain:* MN, SF2, LAI *HIV component:* gp120 MN, gp41 LAI, Gag LAI, partial Pol LAI, rgp120 SF2 *Stimulatory Agents:* MF59

Ab type: V3 **References:** [Verrier (2000)]

- Serum Abs elicited by this vaccine reacted with V3 peptides from clades B, C, and F, reacted weakly with V3 peptides from clades A, D, G, and H, and did not react with V3 peptides from clades E and O – neutralizing activity against 5 of 14 primary isolates tested was observed, including one B clade X4 virus, two dual-tropic B clade viruses, and one clade B and one clade C R5 virus [Verrier (2000)]

868	polyclonal	Env( )	gp120(303–325)	no	*in vitro* stimulation	human(IgM)

Ab type: V3 **References:** [Sidorova(1999)]

- Polyspecific anti-MN-24 antibodies were raised through V3 peptide, MN-24 stimulation of human cells, followed by EBV transformation: they react with homologous and heterologous peptides and may be autoantibodies [Sidorova(1999)]

869	TH1	Env( )	gp120( )	L (MN,JRCSF)		human(IgG1λ)

Ab type: V3 **Donor:** Michael Fung, Tanox Biosystem, USA
References: [D'Souza (1995), Yang (1998)]

- TH1: Found to neutralize MN and JRCSF, but not two B subtype primary isolates, nor a D subtype primary isolate, by most labs in a multi-laboratory study involving 11 labs [D'Souza (1995)]
- TH1: A neutralization assay was developed based on hemi-nested PCR amplification of the LTR (HNPCR) – LTR-HNPCR consistently revealed HIV DNA and was shown to be a rapid, specific and reliable neutralization assay based on tests with 6 MAbs and 5 isolates [Yang (1998)]

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870 11/75a/21/41 Env(dis) gp120(dis) ( )

Ab type: V3 discontinuous **References:** [McKeating (1992a), Peet (1998)]

- 11/75a/21/41: The most variable amino acids in the V3 loop were replaced with serines to make the immunodominant V3 loop less immunogenic – these changes did not affect the ability of sCD4 or MAbs to V1/V2, C1 and C4 to bind, but anti-V3 MAb 11/75a/21/41 binding was dramatically diminished by V3 serine substitutions – mice injected with serine substituted gp120 had a reduced response relative to wildtype, and no enhanced immunogenicity of conserved regions [Peet (1998)]

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871 41.1 (ICR41.1i, ICR41) Env(dis) gp120(dis HXB10) L (HXB2) Vaccine rat(IgG2a)

Vaccine: *Vector/type:* recombinant protein *Strain:* BH10 *HIV component:* gp120

Ab type: V3 discontinuous **Donor:** J. Cordell, Institute for Cancer Research, Sutton, Surrey, UK
References: [McKeating (1992a), McKeating (1993b), Klasse (1993a), McLain & Dimmock(1994), Armstrong & Dimmock(1996), Armstrong (1996), Jeffs (1996), Ugolini (1997)]

- 41.1: The gp41 mutation 582(Ala to Thr) results in conformational changes in gp120 that confer neutralization resistance to conformationally sensitive neutralizing MAbs – neutralization efficiency of 41.1 is not affected [Reitz (1988), Klasse (1993a)]
- 41.1: Called ICR41.1i – Kinetics of neutralization studied – no lag for 39.3b, while ICR 39.13g and ICR 41.1i have lags of 5 and 15 min respectively – neutralization mediated by 3 molecules of IgG per virion – most efficient at neutralization of the three MAbs studied – acts with multi-hit kinetics [McLain & Dimmock(1994)]
- 41.1: Called ICR41.1i – IgG2c? – Neutralization was affected if the Ab was added after the virus bound to the host cells at 24 degrees C or below [Armstrong & Dimmock(1996)]
- 41.1: Called ICR41.1i – Neutralization occurs by blocking a post-fusion internalization event, in contrast to MAb F58 [Armstrong (1996)]
- 41.1: Deletion of the V1V2 regions did not affect anti-V3 Abs ability to bind when compared to intact rec gp120 [Jeffs (1996)]
- 41.1: Viral binding inhibition by 41.1 was weakly correlated with neutralization (all other neutralizing MAbs tested showed some correlation except 2F5) [Ugolini (1997)]

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872 55/45a/1l Env(dis) gp120(dis) ( )

Ab type: V3 discontinuous **References:** [Peet (1998)]

- 55/45a/11: The most variable amino acids in the V3 loop were replaced with serines to make the immunodominant V3 loop less immunogenic – these changes did not affect the ability of sCD4 or MAbs to V1/V2, C1 and C4 to bind, and anti-V3 MAb 55/45a/11 binding was only marginally diminished by V3 serine substitutions – mice injected with serine substituted gp120 had a reduced response relative to wildtype, and no enhanced immunogenicity of conserved regions [Peet (1998)]

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873 1108 Env( ) Env( ) HIV-1 infection human(IgG1λ)

Ab type: V3 mimotype **References:** [Zolla-Pazner (1999a), Zolla-Pazner (1999b)]

- 1108: Selected with peptide 987, a mimotope of anti-V3 MAb 447-D – MAb peptide reactivity pattern clustered with immunological related MAbs: 1108, 386, 268, 311, 257, 694.8 – the amino acids HI tended to be critical for reactivity in this group [Zolla-Pazner (1999b)]
- 1108: The sequence of peptide 987, used to select MAb 1108, is ADGAWRSVHLGPGRGSGSGMGK [Zolla-Pazner (1999a)]

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874 MO101/V3,C4 Env(dis 314–323 + 494–503) gp120(dis 314–323) GRAFVTIGKI + LGVAPTKAKR *in vitro* stimulation human(IgM)

Ab type: V3-C4 **References:** [Ohlin (1992)]

- MO101: Generated in response to IIIB Env 286–467 upon *in vitro* stimulation of uninfected-donor lymphocytes – reacts with peptides 314–323 + 494–503 from the V3 and C4 regions [Ohlin (1992)]

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875 D27 Env(dis) gp120(dis IIIB) Vaccine murine(IgG)

Vaccine: *Vector/type:* vaccinia *Strain:* IIIB *HIV component:* oligomeric gp140

Ab type: V3-CD4BS **Donor:** P. Earl, National Institute of Allergy and Infectious Diseases, NIH, Bethesda, MD
References: [Earl (1994), Otteken (1996), Sugiura (1999)]

- D27: Pulse label experiments of 4 MAbs (D20, D27, T20, and T22) binding to noncleavable gp160 revealed that these anti-CD4 MAbs bound with a delay, and that the epitope formed with a $t_{1/2}$ of about 10 minutes [Otteken (1996)]
- D27: A comparison of 25 gp120 specific, conformation dependent MAbs was done – D27 is one of two MAbs labeled group Ca, that was type-specific for BH8 – D27 fully blocked CD4 binding, and the deletion of the V3 loop abrogated binding [Sugiura (1999)]

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876 D56 Env(dis) gp120(dis IIIB) L Vaccine murine(IgG)

Vaccine: *Vector/type:* vaccinia *Strain:* IIIB *HIV component:* oligomeric gp140

Ab type: V3-CD4BS **Donor:** P. Earl, National Institute of Allergy and Infectious Diseases, NIH, Bethesda, MD
References: [Earl (1994), Sugiura (1999)]

- D56: A comparison of 25 gp120 specific, conformation dependent MAbs was done – D56 is one of two MAbs labeled group Ca, that was type-specific for BH8 – D56 fully blocked CD4 binding, and the deletion of the V3 loop abrogated binding – 12.5 μg/ml of D56 was required to achieve 50% neutralization of HIV-1 NL4–3 [Sugiura (1999)]

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877 polyclonal Env( ) gp120(IIIB) Vaccine rabbit( )

Vaccine: *Vector/type:* peptide *Strain:* MN *HIV component:* gp120 V3/C4 *Stimulatory Agents:* mucosal adjuvant CT

Ab type: V3C4 **References:** [Zinckgraf (1999)]

- Nasal mucosal immunization and boosting of HIV peptide and was superior for inducing serum IgG and vaginal secretory IgA compared to nasal immunization and vaginal boosting – vaginal immunization and boosting resulted low serum IgG and vaginal IgA and a high vaginal IgG response [Zinckgraf (1999)]

878	2G12 (c2G12)	Env(dis)	gp120(dis)	L	P	HIV-1 infection	human(IgG1κ)

Ab type: V3V4, carbohydrates **Donor:** Herman Katinger, Inst. Appl. Microbiol. or Polymun Scientific Inc., Vienna, Austria, MRC AIDS reagent project

References: [Buchacher (1994), Trkola (1995), Moore & Ho(1995), McKeating (1996), McKeating(1996), Trkola (1996b), Moore & Sodroski(1996), Poignard (1996b), Trkola (1996a), Sattentau(1996), D'Souza (1997), Mo (1997), Binley (1997a), Fouts (1997), Li (1997), Moore & Trkola(1997), Mascola (1997), Ugolini (1997), Burton & Montefiori(1997), Parren (1997b), Andrus (1998), Wyatt (1998), Mondor (1998), Parren (1998a), Sullivan (1998b), Connor (1998), Binley (1998), Trkola (1998), Fouts (1998), Takefman (1998), Parren (1998b), Li (1998), Wyatt & Sodroski(1998), Frankel (1998), Kunert (1998), Schonning (1998), Montefiori & Evans(1999), Beddows (1999), Altmeyer (1999), Poignard (1999), Parren (1999), Mascola (1999), Mascola (2000), Binley (1999), Baba (2000), Grovit-Ferbas (2000), Park (2000), Mascola & Nabel(2001), Zwick (2001c), Barnett (2001), Moore (2001), Poignard (2001), Zeder-Lutz (2001), Verrier (2001), Stiegler (2001), Spenlehauer (2001), Hofmann-Lehmann (2001), Xu (2001), Savarino (2001), Armbruster (2002)]

- 2G12: Human MAb generated by electrofusion of PBL from HIV-1+ volunteers with CB-F7 cells [Buchacher (1994)]
- 2G12: Highly potent Cross-clade neutralizing activity [Trkola (1995)]
- 2G12: Conformationally sensitive epitope destroyed by mutations altering the N-linked glycosylation sites near the base of the V3 loop and the amino-terminal flank of the V4 loop [Trkola (1996b)]
- 2G12: Binding weakly enhanced by some anti-C1, -C4, -V3, and CD4 binding site MAbs – unusual in that 2G12 binding neither enhanced or inhibited the binding of other MAbs included in the study [Moore & Sodroski(1996)]
- 2G12: Review: binding site is distinct from CD4BS MAbs epitope and is unique among known gp120 MAbs, human or rodent [Moore & Ho(1995)]
- 2G12: Review: exceptional capacity to neutralize primary isolates in terms of both breadth and potency – one of three MAbs (IgG1b12, 2G12, and 2F5) generally accepted as having significant potency against primary isolates [Poignard (1996b)]
- 2G12: Neutralizes JR-FL – inhibits gp120 interaction with CCR-5 in a MIP-1β-CCR-5 competition study [Trkola (1996a)]
- 2G12: Neutralizes primary isolates, HXB2, and chimeric virus with gp120 from primary isolates in an HXB2 background [McKeating (1996)]
- 2G12: Review: Only four epitopes have been described which can stimulate a useful neutralizing response to a broad spectrum of primary isolates, represented by the binding sites of MAbs: 447-52-D, 2G12, Fab b12, and 2F5 [Sattentau(1996)]
- 2G12: In a multilab evaluation of monoclonal antibodies, only IgG1b12, 2G12, and 2F5 could neutralize at least half of the 9 primary test isolates at a concentration of < 25 μg per ml for 90% viral inhibition – neutralized 6 of 9 primary isolates [D'Souza (1997)]
- 2G12: A JRCSF variant that was selected for IgG1b12 resistance remained sensitive to MAbs 2G12 and 2F5, for combination therapy [Mo (1997)]
- 2G12: Study shows neutralization is not predicted by MAb binding to JRFL monomeric gp120, but is associated with oligomeric Env binding – 2G12 bound monomer, and weakly bound oligomer and neutralized JRFL [Fouts (1997)]
- 2G12: One of 14 human MAbs tested for ability to neutralize a chimeric SHIV-vpu+, which expressed HIV-1 IIIB Env – 2G12 was a strong neutralizer of SHIV-vpu+ – all Ab combinations tested showed synergistic neutralization – 2G12 has synergistic response with MAbs 694/98-D (anti-V3), 2F5, F105, and b12 [Li (1997)]

- 2G12: Review: MABs 2F5, 2G12 and IgG1b12 have potential for use in combination with CD4-IgG2 as an immunotherapeutic or immunoprophylactic – homologous MAbs to these are rare in humans and vaccine strategies should consider including constructs that may enhance exposure of these MAbs' epitopes [Moore & Trkola(1997)]
- 2G12: Using concentrations of Abs achievable *in vivo*, the triple combination of 2F5, 2G12 and HIVIG was found to be synergistic to have the greatest breadth and magnitude of response against 15 clade B primary isolates [Mascola (1997)]
- 2G12: Viral binding inhibition by 2G12 was strongly correlated with neutralization (all other neutralizing MAbs tested showed some correlation except 2F5) [Ugolini (1997)]
- 2G12: Review that discusses this MAb – reacts with residues at the base of the V3 loop and V4, and most of the changes that reduce binding are glycosylation sites – it is not clear whether the binding site is peptidic or direct carbohydrate [Burton & Montefiori(1997)]
- 2G12: Neutralizes TCLA strains and primary isolates [Parren (1997b)]
- 2G12: Post-exposure prophylaxis was effective when MAb 694/98-D was delivered 15 min post-exposure to HIV-1 LAI in hu-PBL-SCID mice, but declined to 50% if delivered 60 min post-exposure, and similar time constraints have been observed for HIVIG, 2F5 and 2G12, in contrast to MAb BAT123 that could protect delivered 4 hours post infection [Andrus (1998)]
- 2G12: The MAb and Fab binding to the oligomeric form of gp120 and neutralization were highly correlated – authors suggest that neutralization is determined by the fraction of Ab sites occupied on a virion irrespective of the epitope [Parren (1998a)]
- 2G12: Summary of the implications of the crystal structure of gp120 combined with what is known about mutations that reduce NAb binding – probable mechanism of neutralization by 2G12 is unknown, but dependent on proper glycosylation and 2G12 is predicted to be oriented towards the target cell when bound, so neutralization may be due to steric hindrance – mutations in positions N 295, T 297, S 334, N 386, N 392 and N 397 HXBc2 (IIIB) decrease 2G12 binding, and the binding region is 25 angstroms from the CD4 binding site – probably the Ab binds in part to carbohydrates, which may account for both its broad reactivity and the scarcity of Abs in the same competition group [Wyatt (1998)]
- 2G12: Enhances Hx10 binding to CD4 positive or negative HeLa cells, but inhibited binding to CD4+ T-cell line A3.01 – neutralizes Hx10 infection of the HeLa cells [Mondor (1998)]
- 2G12: Ab from gp120 vaccinated individuals prior to infection, who subsequently became HIV infected, could not achieve 90% neutralization of the primary virus by which the individuals were ultimately infected – these viruses were not particularly refractive to neutralization, as determined by their susceptibility to neutralization by MAbs 2G12, IgG1b12, 2F5 and 447-52D [Connor (1998)]
- 2G12: Does not compete with binding of MAb generated in response to gp120-CD4 complex, CG10 [Sullivan (1998b)]
- 2G12: A panel of MAbs were shown to bind with similar or greater affinity and similar competition profiles to a deglycosylated or variable loop deleted core gp120 protein (Δ V1, V2, and V3), thus such a core protein produces a structure closely approximating full length folded monomer – MAb 2G12 was the only exception to this, showing reduced binding efficiency [Binley (1998)]
- 2G12: A wide range of neutralizing titers was observed that was independent of co-receptor usage [Trkola (1998)]
- 2G12: Notes that 2G12 and 2F5, potent neutralizing antibodies, were identified by screening for cell surface (oligomeric Envelope) reactivity [Fouts (1998)]
- 2G12: Induces Complement-mediated lysis in MN but not primary isolates – primary isolates are refractive to CML [Takefman (1998)]

- 2G12: MAbs 2G12, 2F5 and b12 are broadly neutralizing, as are some human polyconal sera, but this paper describes a set of primary isolates that are resistant to all three MAbs and 2 broadly neutralizing sera – results indicate that resistance levels of pediatric isolates might be higher than adult isolates – resistance in general did not seem to be conferred by a loss of binding affinity for gp120 or gp41, rather by a more global perturbation of oligomeric Envelope [Parren (1998b)]
- 2G12: Neutralization synergy was observed when the MAbs 694/98-D (V3), 2F5 (gp41), and 2G12 (gp120 discontinuous) were used in combination, and even greater neutralizing potential was seen with the addition of a fourth MAb, F105 (CD4 BS) [Li (1998)]
- 2G12: Discussed in a review of the antigenic and receptor binding-domains of gp120 in relation to the structure of the molecule – antibodies are discussed by category (anti-V2, anti-V3, CD4i, CD4BS...), however as 2G12 binds to a rarely immunogenic region, and it is dependent on glycosylation, it was discussed individually [Wyatt & Sodroski(1998)]
- 2G12: The complete V, J and D(H) domain was sequenced – unlike non-neutralizing anti-gp41 MAb 3D6, five neutralizing MAbs (2F5, 2G12, 1B1, 1F7, and 3D5) showed extensive somatic mutations giving evidence of persistent antigenic pressure over long periods – 2G12 D(H) has the best homology to a D(H) segment between D3–22 and D4–23, a region not usually considered for heavy-chain rearrangement because it lacks associated recombination signals in the flanking regions, Kunert *et al*. suggest this may be why Abs that compete with 2G12 are rare [Kunert (1998)]
- 2G12: In a study of the influence of the glycan at position 306 of the V3 loop on MAb recognition, 2G12 was found to neutralize an HIV-BRU mutant virus that lacks the V3 loop glycan and has a mutation at the tip of the loop more efficiently than it neutralizes HIV-BRU [Schonning (1998)]
- 2G12: Infection of dendritic cells cultured from CD14+ blood cells or from cadaveric human skin was blocked by neutraling MAbs IgG1b12, or 2F5 and 2G12 delivered together, but not by control non-neutralizing anti-gp120 MAb 4.8D, indicating that NAbs could interrupt early mucosal transmission events [Frankel (1998)]
- 2G12: A meeting summary presented results regarding neutralization –MAbs 2G12 and 2F5 tested for their ability to neutralize primary isolate infection of genetically engineered cell lines (cMAGI and others, presented by T. Matthews, A. Trkola, J. Bradac) – an advantage of such cells lines over PBMCs is that markers (X-Gal) can be added for staining to simplify the assay – the consensus of the meeting was that these engineered cell lines did not improve the sensitivity of detection of primary isolate neutralization – D. Burton and J. Mascola presented results concerning passive immunization and protection of hu-PBL-SCID mice and macaques, respectively, and both found combinations of MAbs that were able to achieve 99% neutralization *in vitro* corresponded to efficacy *in vivo* [Montefiori & Evans(1999)]
- 2G12: rgp120 derived from a R5X4 subtype B virus was used to vaccinate healthy volunteers and the resulting sera were compared with sera from HIV-1 positive subjects and neutralizing MAbs – 2G12 was able to bind with low affinity to the rgp120 monomer HIV-1 W61D [Beddows (1999)]
- 2G12: A Semliki Forest virus (SFV) expression system carrying BX08 Env was used to study the conformation of gp120 Env – intracytoplasmic gp120 was recognized by the anti-V3 MAbs K24 and F5.5, while gp120 at the plasma membrane was detected only by conformation dependent MAbs 2G12, 670-D and 694/98D and not V3 MAbs – expression in rat brain also showed that surface expressed Env was recognized only by the conformation-dependent antibodies and not by anti-V3 antibodies [Altmeyer (1999)]

- 2G12: Hu-PBL-SCID mice were infected with HIV-1s JRCSF and SF162 to study the effect of NAbs on an established infection – no significant differences in the initial rate of decrease in viral load or the plateau levels of viral RNA between the b12 treated and control mice were seen – in most of the Ab treated mice b12 escape mutants were observed with varying patterns of mutations – a combination of b12, 2G12 and 2F5 protected 1/3 mice, and an isolate from one of the other two was resistant to neutralization by all three MAbs [Poignard (1999)]
- 2G12: Review of the neutralizing Ab response to HIV-1 [Parren (1999)]
- 2G12: Combinations of HIVIG, 2F5, 2G12 were administered in passive-transfer experiments 24 hours prior to challenge with pathogenic SHIV 89.6PD – 3/6 animals given HIVIG/2F5/2G12 were completely protected, the others had reduced viremia and normal CD4 counts – 1/3 monkeys given 2F5/2G12 showed transient infection, the other two had reduced viral load – all monkeys that received HIVIG, 2F5, or 2G12 alone became infected and developed high-level plasma viremia, although animals that got HIVIG or 2G12 had a less profound CD4 T cell decline [Mascola (1999)]
- 2G12: Because HIV-1 is most often transmitted across mucosal surfaces, the ability of passive transfer of infused HIVIG/2F5/2G12 to protect against mucosal exposure of macaques to pathogenic SHIV 89.6PD was studied – HIVIG/2F5/2G12 protected 4/5 animals against vaginal challenge, 2F5/2G12 combined protected 2/5 animals, and 2G12 alone protected 2/4 animals – in contrast, Mascola and co-workers had previously shown single MAbs could not protect against intervenous challenge – Ab treated animals that got infected through vaginal innoculation had low viral loads and only modest declines in CD4 counts – the infused Abs were detected in the nasal, vaginal, and oral mucosa [Mascola (2000)]
- 2G12: Combinations of HIVIG, 2F5, 2G12 were administered in passive-transfer experiments 24 hours prior to challenge with pathogenic SHIV 89.6PD – 3/6 animals given HIVIG/2F5/2G12 were completely protected, the others had reduced viremia and normal CD4 counts – 1/3 monkeys given 2F5/2G12 showed transient infection, the other two had reduced viral load – all monkeys that received HIVIG, 2F5, or 2G12 alone became infected and developed high-level plasma viremia, although animals that got HIVIG or 2G12 had a less profound CD4 T cell decline [Mascola (1999)]
- 2G12: The MAbs with the broadest neutralizing activity, IgG1b12, 2G12 and 2F5, all have high affinity for the native trimer, indicating that they were raised in an immune response to the oligomer on the virion surface rather than dissociated subunits – a disulfide linked gp120-gp41 (SOS gp140) was created to mimic the native conformation of Env and explore its potential as an immunogen – SOS gp140 is recognized by NAbs IgG1b12, 2G12, and CD4-IgG2, and also by anti-V3 MAbs 19b and 83.1 – SOSgp140 is not recognized by C4 region MAbs that neutralize only TCLA strains, G3-42 and G3-519 – nor did it bind C11, 23A, and M90, MAbs that bind to gp120 C1 and C5, where it interacts with gp41 – MAbs that bind CD4 inducible epitopes, 17b and A32 were very strongly induced by CD4 in SOS gp140 – anti-gp41 MAbs that bind in the region that interacts with gp120, 7B2, 2.2B, T4, T15G1 and 4D4, did not bind to SOSgp140, in contrast to 2F5, which binds to the only gp41 epitope that is well exposed in native gp120-gp41 complexes [Binley (1999)]
- 2G12: A triple combination of 2F5, F105 and 2G12 effectively neutralized perinatal infection of macaque infants when challenged with SHIV-vpu+ – the mean plasma half-life of 2G12 was 14.0 $\pm$ 7.9 days, the longest of the three Abs [Baba (2000)]
- 2G12: To determine the antigenicity of virus killed by thermal and chemical inactivation, retention of conformation-dependent neutralization epitopes was examined, and exposure of CD4BS epitopes was found to be enhanced (MAbs IgG1b12, 205-46-9, and 205-43-1) – binding to 2G12 and 447-52D epitopes was essentially unaltered – the 17b CD4i epitope was also exposed [Grovit-Ferbas (2000)]

- 2G12: Six mutations in MN change the virus from a high-infectivity neutralization resistant phenotype to low-infectivity neutralization sensitive – V3, CD4BS, and CD4i MAbs are 20–100 fold more efficient at neutralizing the sensitive form – 2G12 was an exception and could not neutralize MN in either form [Park (2000)]
- 2G12: Neutralization synergy between anti-HIV NAbs b12, 2G12, 2F5, and 4E10 was studied – a classic fixed-ratio method was used, as well as a method where one Ab was fixed at a low neutralization titer and the other was varied – using primary isolates, a two-four fold enhancement of neutralization was observed with MAb pairs, and a ten-fold enhancement with a quadruple Ab combination – no synergy was observed with any MAb pair in the neutralization of TCLA strain HXB2 – there was no evidence for cooperativity of binding between b12 and 2G12 to envelope spikes expressed on the cell surface of TCLA or primary isolates [Zwick (2001c)]
- 2G12: Review of studies in macaques that have shown immune control of pathogenic SHIV viremia, improved clinical outcome, and protection, and the implications of the observations for HIV vaccines [Mascola & Nabel(2001)]
- 2G12: SF162ΔV2 is a virus that has a 30 amino acid deletion in the V2 loop that does not abrogate its infectivity but renders it highly susceptible to neutralization – when incorporated into a codon-optimized DNA vaccine with a CMV promoter and delivered by gene gun, SF162ΔV2 gave higher neutralizing Ab titers against SF162 than did SF162 itself, and Abs that cross-neutralized non-homologous primary isolates were obtained only when SF162ΔV2, but not intact SF162, was used as the immunogen – Control MAbs 2F5 and 2G12 could neutralize all of the following primary isolates: 91US056(R5), 92US714(R5), 92US660(R5), 92HT593(R5X4), and BZ167(R5X4), while after the first protein boost, the sera from two SF162ΔV2 immunized macaques could neutralize 91US056(R5), 92US714(R5), 92US660(R5) and ADA(R5), but not 92HT593(R5X4) or 92US657(R5) – the pattern of cross-recognition shifted after the second boost [Barnett (2001)]
- 2G12: Moore and colleagues review structural aspects of gp120 and how they relate to antigenic domains, and review the data concerning the lack of a clear relationship between genetic subtype and serotype – an exception exists for human MAb 2G12, which does not recognize CRF01 envelopes because of an unusual additional disulfide bond in the V4 loop region that appears to be unique to the subtype E, CRF01 gp120 protein [Moore (2001)]
- 2G12: Structural aspects of the interaction of neutralizing Abs with HIV-1 Env are reviewed – Env essentially has three faces, one is largely inaccessible on the native trimer, and two that exposed but have low immunogenicity on primary viruses – neutralization is suggested to occur by inhibition of the interaction between gp120 and the target cell membrane receptors as a result of steric hindrance and it is noted that the attachment of approximately 70 IgG molecules per virion is required for neutralization, which is equivalent to about one IgG molecule per spike – the 2G12, 17b and b12 epitopes are discussed in detail – although it is potently neutralizing, 2G12 does not interfere with CD4 and coreceptor binding, and this Ab specificity is uncommon in sera from HIV-1-infected individuals [Poignard (2001)]
- 2G12: Neutralizing synergy between MAbs 1b12, 2G12 and 2F5 was studied using surface plasmon resonance to determine the binding kinetics for these three MAbs with respect to monomeric and oligomeric Env protein gp160 IIIB – the 2G12 epitope is highly accessible on both monomeric and oligomeric Envs, 1b12 is highly accessible on monomers but not oligomers, and 2F5 on neither form – binding of 2G12 exposes the 2F5 epitope on gp160 oligomers – 2G12-gp160 oligomer interactions were best fitted to a two state model, with the first complex having a high association constant and fast dissociation, that is stabilized by conformational changes induced by the binding of a second MAb [Zeder-Lutz (2001)]
- 2G12: A luciferase-reporter gene-expressing T-cell line was developed to facilitate neutralization and drug-sensitivity assays – luciferase and p24 antigen neutralization titer end points were found comparable using NAb from sera from HIV+ donors, and MAbs 2F5, 2G12 and IgG1b12 [Spenlehauer (2001)]

- 2G12: A panel of 12 MAbs was used to identify those that could neutralize the dual-tropic primary isolate HIV-1 89.6 – six gave significant neutralization at 2 to 10 μg/ml: 2F5, 50–69, IgG1b12, 447-52D, 2G12, and 670-D – six did not have neutralizing activity: 654-D, 4.8D, 450-D, 246-D, 98–6, and 1281 – no synergy, only additive effects were seen for pairwise combinations of MAbs, and antagonism was noted between gp41 MAbs 50–69 and 98–6, as well as 98–6 and 2F5 [Verrier (2001)]
- 2G12: A combination of MAbs IgG1b12, 2F5, and 2G12 was given postnatally to four neonate macaques that were then challenged with highly pathogenic SHIV89.6P – one of the four infants remained uninfected after oral challenge, two infants had no or a delayed CD4(+) T-cell decline [Hofmann-Lehmann (2001)]
- 2G12: Twenty HIV clade C isolates from five different countries were susceptible to neutralization by anti-clade B MAbs in a synergistic quadruple combination of mAbs IgG1b12, 2G12, 2F5, and 4E10 [Xu (2001)]
- 2G12: Chloroquine reduces the HIV-1-infectivity of H9 IIIB cells, apparently through altering the conformation of envelope – there is a a reduction of reactivity of 2G12 to its epitope in chloroquine treated cultures [Savarino (2001)]
- 2G12: A phase I trial in seven HIV+ individuals was conducted with MAbs 2F5 and 2G12 – no clinical or laboratory abnormalities were observed throughout the study – eight infusions were administered over a 4-week period – the elimination half-life ($t_{1/2}$) was calculated to be 7.94 (range, 3.46–8.31) days for 2F5 and 16.48 (range, 12.84–24.85) days for 2G12 [Armbruster (2002)]
- 2G12: UK Medical Research council AIDS reagent: ARP3030
- 2G12: NIH AIDS Research and Reference Reagent Program: 1476

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879 MO101/V3,C4 Env(dis 314–323 + 494–503) gp120(dis 314–323) GRAFVTIGKI + LGVAPTKAKR *in vitro* stimulation human(IgM)

Ab type: V3-C5 **References:** [Ohlin (1992)]

- MO101: Generated through *in vitro* stimulation of uninfected-donor lymphocytes with pB1 containing IIIB Env 286–467 – reacts with peptides from the V3 and C4 regions, positions 314–323 + 494–503, peptides GRAFVTIGKI + LGVAPTKAKR [Ohlin (1992)]

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881 Env( ) gp120(IIIB) Vaccine murine(IgG1)

Vaccine: *Vector/type:* vaccinia *Strain:* IIIB *HIV component:* gp120 *Stimulatory Agents:* GM-CSF

References: [Rodriguez (1999)]

- The murine antibody response to a chimeric of granulocyte-macrophage colony stimulating factor GM-CSF/gp120 in vaccinia was not higher titer that the response to a gp120-vaccinia construct, but the breadth of the antibody response was greater, in particular to the C-term region of gp120
- A cellular response of greater intensity was trigged to the GM-CSF/gp120 vaccinia construct, as measured by gamma IFN production in an Elispot assay

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882 102–135 Env(dis 549–673) gp41(dis HAM112, O group) Vaccine murine(IgG1κ)

Vaccine: *Vector/type:* recombinant protein *Strain:* HAM112 (group O) *HIV component:* gp160

References: [Scheffel (1999)]

- 102–135: Overlapping peptides based on group O HAM112 Env were tested for MAb reactivity – 102–135 bound to two non-contiguous peptides in combination, assumed to combine to form some type of helical structure, and not to either peptide individually [Scheffel (1999)]

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883 1025 Env(dis) gp120(dis) ( )

References: [Berman (1997)]

- 1025: Binds to 1/7 isolates from breakthrough cases from a MN gp120 vaccine trial [Berman (1997)]

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884 105–134 Env( ) gp41(652–681 HAM112, O group) Vaccine murine(IgG1κ)

Vaccine: *Vector/type:* recombinant protein *Strain:* HAM112 (group O) *HIV component:* gp160

References: [Scheffel (1999)]

- 105–134: Overlapping peptides based on group O HAM112 Env were tested for MAb reactivity [Scheffel (1999)]

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885 10E9 Env( ) gp41( ) HIV-1 infection murine(IgG1)

References: [Papsidero (1988)]

- 10E9: 100/100 HIV+ human sera could inhibit 10E9 binding [Papsidero (1988)]

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886 126–50 Env(dis) gp41(dis HXB2) no HIV-1 infection human(IgG2κ)

References: [Robinson (1990b), Tyler (1990), Robinson (1991), Xu (1991)]

- 126–50: No enhancing activity for HIV-1 IIIB [Robinson (1990b)]
- 126–50: Serves as target for antibody-dependent cellular cytotoxicity ADCC [Tyler (1990)]
- 126–50: No enhancing or neutralizing activity [Robinson (1991)]
- 126–50: Specific for a conformational epitope [Xu (1991)]

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887 12H2 Env(dis 530–677) gp41(dis 530–677 HXB2) no Vaccine murine(IgMκ)

Vaccine: *Vector/type:* Semliki-Forest Virus *HIV component:* Env

References: [Giraud (1999)]

- 12H2: Env in a Semliki-Forest Virus (SFV) vector was used to vaccinate mice intramuscularly as naked RNA, and an Ab response was induced to Env from which 12H2 was derived – and advantage of this method is that the protein is properly expressed [Giraud (1999)]

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888 13.10 (No. 13) | Env( ) | gp120( ) | no | HIV-1 infection | human(IgG1λ)

Donor: Evan Hersh and Yoh-Ichi Matsumoto
References: [Lake (1989), Moran (1993), Wisnewski (1996)]

- 13.10: First HIV-1 specific human-mouse hybridoma that produces a MAb that binds to gp120 and gp160 [Lake (1989)]
- 13.10: Heavy (V HI) and light (V λII) chain sequenced – no enhancing or neutralizing activity – called No. 13 [Moran (1993)]
- 13.10: 13.10 is V H1 – V-region heavy chain usage was examined and a bias of enhanced V H1 and V H4, and reduced V H3, was noted among HIV infected individuals [Wisnewski (1996)]
- 13.10: NIH AIDS Research and Reference Reagent Program: 377

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889 1B1 | Env( ) | Env( ) | L | HIV-1 infection | human( )

Donor: Herman Katinger, Inst. Appl. Microbiol. University of Agricultural Science, Vienna, Austria
References: [Buchacher (1994), Purtscher (1994), Kunert (1998)]

- 1B1: Generated by electrofusion of PBL from HIV-1 positive volunteers with CB-F7 cells [Buchacher (1994)]
- 1B1: The complete V, J and D(H) domain was sequenced – unlike non-neutralizing anti-gp41 MAb 3D6, five neutralizing MAbs (2F5, 2G12, 1B1, 1F7, and 3D5) showed extensive somatic mutations giving evidence of persistent antigenic pressure over long periods [Kunert (1998)]

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890 1F7 | Env( ) | Env( ) | L | HIV-1 infection | human( )

Donor: Herman Katinger, Inst. Appl. Microbiol. University of Agricultural Science, Vienna, Austria
References: [Buchacher (1994), Purtscher (1994), Kunert (1998), Grant (2000)]

- 1F7: Generated by electrofusion of PBL from HIV-1 positive volunteers with CB-F7 cells [Buchacher (1994)]
- 1F7: The complete V, J and D(H) domain was sequenced – unlike non-neutralizing anti-gp41 MAb 3D6, five neutralizing MAbs (2F5, 2G12, 1B1, 1F7, and 3D5) showed extensive somatic mutations giving evidence of persistent antigenic pressure over long periods [Kunert (1998)]
- 1F7: There is an anti-idiotype MAb named 1F7 that was raised against pooled IgG from HIV-1+ subjects that recognizes a set of antibodies against HIV Gag, Pol, and Env, and this MAb is reported to inhibit anti-HIV CTL activity – this is not the same as the 1F7 described by Buchacher *et al*. [Grant (2000)]

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891 31710B | Env( ) | gp41( ) | human(IgG1)

References: [Alsmadi & Tilley(1998)]

- 31710B: A study of 6 anti-Env MAbs and their ability to bind or direct ADCC against target cells infected with IIIB, MN, SF-2, and RF – bound and directed lysis against all four strains [Alsmadi & Tilley(1998)]

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892 3D5 | Env( ) | Env( ) | L | HIV-1 infection | human( )

Donor: Herman Katinger, Inst. Appl. Microbiol. University of Agricultural Science, Vienna, Austria
References: [Buchacher (1994), Purtscher (1994), Kunert (1998)]

- 3D5: Generated by electrofusion of PBL from HIV-1 positive volunteers with CB-F7 cells [Buchacher (1994)]

- 3D5: The complete V, J and D(H) domain was sequenced – unlike non-neutralizing anti-gp41 MAb 3D6, five neutralizing MAbs (2F5, 2G12, 1B1, 1F7, and 3D5) showed extensive somatic mutations giving evidence of persistent antigenic pressure over long periods [Kunert (1998)]

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893 3H6 Env( ) gp41( ) murine( )

References: [Pinter (1995)]

- 3H6: There is another MAb with this ID that recognizes Rev [Orsini (1995)]
- 3H6: Generated in response to virus grown in protein-free medium [Pinter (1995)]

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894 6E10 Env(dis) gp120(dis) L Vaccine ( )

Vaccine: *Vector/type:* recombinant protein *HIV component:* gp160

Donor: Phil Berman

References: [Berman (1991)]

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895 7–1054 Env( ) gp36(HIV-2) no murine( )

References: [Scheffel (1999)]

- Binds HIV-2 gp36, used as a control in a study of group O MAbs [Scheffel (1999)]

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896 A9 Env( ) gp120(IIIB) Vaccine murine(IgG1)

Vaccine: *Vector/type:* chimeric GM-CSF *Strain:* IIIB *HIV component:* gp120 *Stimulatory Agents:* GM-CSF

References: [del Real (1999)]

- A9: Murine antibody response to the chimeric construction granulocyte-macrophage colony stimulating factor GM-CSF/gp120 was tested, MAbs from normal mice were gp120 specific, MAbs from nude mice bound gp120 but were polyreactive, and from reconstituted mice were half way between – the anti-gp120 response used a high frequency of VH81X, VHQ52, and VH7183 genes, a family used during fetal life and associated with autoimmunity – A9 was a gp120 from a BALBc reconstructed nude mouse and had VH gene 7183–2 [del Real (1999)]

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897 B4 Env( ) gp120(IIIB) Vaccine murine(IgM)

Vaccine: *Vector/type:* chimeric GM-CSF *Strain:* IIIB *HIV component:* gp120

References: [del Real (1999)]

- B4: Murine antibody response to the chimeric construction granulocyte-macrophage colony stimulating factor GM-CSF/gp120 was tested, MAbs from normal mice were gp120 specific, MAbs from nude mice bound gp120 but were polyreactive, and from reconstituted mice were half way between – the anti-gp120 response used a high frequency of VH81X, VHQ52, and VH7183 genes, a family used during fetal life and associated with autoimmunity – B4 was an anti-gp120 from a BALBc reconstructed nude mouse and had VH gene J606 [del Real (1999)]

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898 B5 Env( ) gp120(IIIB) Vaccine murine(IgG1)

Vaccine: *Vector/type:* chimeric GM-CSF *Strain:* IIIB *HIV component:* gp120 *Stimulatory Agents:* GM-CSF

References: [del Real (1999)]

- B5: Murine antibody response to the chimeric construction granulocyte-macrophage colony stimulating factor GM-CSF/gp120 was tested, MAbs from normal mice were gp120 specific, MAbs from nude mice bound gp120 but were polyreactive, and from reconstituted mice were half way between – the anti-gp120 response used a high frequency of VH81X, VHQ52, and VH7183 genes, a family used during fetal life and associated with autoimmunity – B5 was a gp120 specific MAb from a BALBc mouse and had VH gene J558 [del Real (1999)]

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899 B6 Env( ) gp120(IIIB) Vaccine murine(IgM)

Vaccine: *Vector/type:* chimeric GM-CSF *Strain:* IIIB *HIV component:* gp120

References: [del Real (1999)]

- B6: Murine antibody response to the chimeric construction granulocyte-macrophage colony stimulating factor GM-CSF/gp120 was tested, MAbs from normal mice were gp120 specific, MAbs from nude mice bound gp120 but were polyreactive, and from reconstituted mice were half way between – the anti-gp120 response used a high frequency of VH81X, VHQ52, and VH7183 genes, a family used during fetal life and associated with autoimmunity – B6 was a gp120 from a BALBc reconstructed nude mouse and had VH gene J558 [del Real (1999)]

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900 BAT267 Env( ) gp120( ) L Vaccine murine(IgG1)

Vaccine: *Vector/type:* inactivated virus *Strain:* IIIB *HIV component:* virus

References: [Fung (1987)]

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901 BAT401 Env( ) gp120( ) L Vaccine murine(IgG1)

Vaccine: *Vector/type:* inactivated virus *Strain:* IIIB *HIV component:* virus

References: [Fung (1987)]

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902 BAT509 Env( ) gp120( ) L Vaccine murine(IgG1)

Vaccine: *Vector/type:* inactivated virus *Strain:* IIIB *HIV component:* virus

References: [Fung (1987)]

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903 C31 Env( ) gp120( ) no HIV-1 infection human(IgG1κ)

References: [Boyer (1991)]

- C31: Broadly-reactive group specific MAb – high yield cultivation of human MAb [Boyer (1991)]

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904 D1 Env(dis) gp41(dis IIIB) Vaccine murine(IgG)

Vaccine: *Vector/type:* vaccinia *Strain:* IIIB *HIV component:* oligomeric gp140

References: [Otteken (1996)]

- D1: MAbs D1, D16, had T37 bind to oligomeric gp160 equally well – pulse label experiments of MAb binding to noncleavable gp160 revealed that these MAbs bound with a delay, epitopes forming with a half-life of 30 min [Otteken (1996)]

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905 D12 Env(dis) gp41(dis IIIB) L Vaccine murine(IgG)

Vaccine: *Vector/type:* vaccinia *Strain:* IIIB *HIV component:* oligomeric gp140

References: [Broder (1994), Richardson (1996), Earl (1997), Otteken (1996), LaBranche (1999)]

- D12: One of 18 MAbs (*e.g.* D4 and D40) that bind to a conformation-dependent epitope in gp41 that bind preferentially, but not exclusively, to oligomers – neutralizes IIIB and SF2 [Broder (1994)]
- D12: This antibody was blocked more strongly by human sera than other anti-gp41 MAbs (D20, D43, D61, and T4) in a oligomeric ELISA assay [Richardson (1996)]
- D12: MAbs D10 and D12 are very easily blocked by human sera from HIV+ individuals [Earl (1997)]
- D12: MAbs D4, D10, D11, D12, and D41 all bind only to complete oligomer – pulse label experiments of MAb binding to noncleavable gp160 revealed that these MAbs bound with a delay, epitopes forming with a half-life of 30 min [Otteken (1996)]
- D12: D12 was used in WB of HIV-1 transmembrane proteins in a study which showed that determinants of HIV-1 CD4 independence map outside regions required for coreceptor specificity – IIIBx, a CD4-independent variant of IIIB, has a truncated gp41 [LaBranche (1999)]

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906 D16 Env(dis) gp41(dis IIIB) L Vaccine murine(IgG)

Vaccine: *Vector/type:* protein *HIV component:* dimeric Env

References: [Earl (1994), Weissenhorn (1996), Earl (1997)]

- D16: Precipitates both oligomeric gp140 and soluble monomeric gp41(21–166)that lacks the fusion peptide and membrane anchor, along with MAbs D16, D38, D40, D41, and D54 [Weissenhorn (1996)]
- D16: One of eleven MAbs (D16, D17, D31, D36, D37, D40, D44, D55, D59, T37, and T45) that are conformation dependent and that can block the binding of the MAb D50 that binds to the linear peptide gp41(642–665) – reactive with 9/10 HIV-1 strains all except HIV-1 ADA, which has the change E659D and E662A that may result in the loss of binding (ELLE to DLLA) [Earl (1997)]

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907 D4 Env( ) gp120(IIIB) Vaccine murine(IgG1)

Vaccine: *Vector/type:* chimeric GM-CSF *Strain:* IIIB *HIV component:* gp120

References: [del Real (1999)]

- D4: Murine antibody response to the chimeric construction granulocyte-macrophage colony stimulating factor GM-CSF/gp120 was tested, MAbs from normal mice were gp120 specific, MAbs from nude mice bound gp120 but were polyreactive, and from reconstituted mice were half way between – the anti-gp120 response used a high frequency of VH81X, VHQ52, and VH7183 genes, a family used during fetal life and associated with autoimmunity – D4 was a gp120 from a BALBc reconstructed nude mouse and had VH gene J558 [del Real (1999)]

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908 D43 Env(dis) gp41(dis HXB2) Vaccine murine(IgG)

Vaccine: *Vector/type:* protein *HIV component:* dimeric Env

References: [Earl (1994), Richardson (1996), Earl (1997)]

- D43: This is a linear gp41 epitope, mapping in the region 635–678 – human sera blocked binding in oligomeric ELISA assay to a similar extent for gp41 MAbs D20, D43, D61, and T4 [Richardson (1996)]

- D43: Partially conformation dependent – doesn‘t bind to short peptides, but does bind to the region spanning 641–683 – binding can be blocked by MAbs T3, D38 and D45 – MAbs in this competition group reacted with 9/10 HIV-1 strains, not binding to JRFL [Earl (1997)]

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909 F223 Env( ) gp120( ) no HIV-1 infection human(IgG3λ)

References: [Cavacini (1999)]

- F223: binds to HIV-1 gp120 – also binds to uninfected lymphocytes, binding to a 159-kd auto-antigen expressed on most B cells and a small fraction of T and NK cells – the antibody enhances HIV-1 infection in a complement-dependent manner – F223 light chains have a strong homology with VLgamma2, the heavy chain to the germline gene VH3-H.11 – N-linked carbohydrates are key for recognition of both gp120 and the autoantigen – MAb 3D6 also uses VH3 and has autoreactivity [Cavacini (1999)]

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910 F285 Env( ) Env( ) HIV-1 infection human(IgG1)

References: [Wisnewski (1995), Wisnewski (1996)]

- F285: F285 is V H1 – V-region heavy chain usage was examined and a bias of enhanced V H1 and V H4, and reduced V H3, was noted among HIV infected individuals [Wisnewski (1996)]

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911 F7 Env( ) gp120(IIIB) Vaccine murine(IgG1)

Vaccine: *Vector/type:* chimeric GM-CSF *Strain:* IIIB *HIV component:* gp120 *Stimulatory Agents:* GM-CSF

References: [del Real (1999)]

- F7: Murine antibody response to the chimeric construction granulocyte-macrophage colony stimulating factor GM-CSF/gp120 was tested, MAbs from normal mice were gp120 specific, MAbs from nude mice bound gp120 but were polyreactive, and from reconstituted mice were half way between – the anti-gp120 response used a high frequency of VH81X, VHQ52, and VH7183 genes, a family used during fetal life and associated with autoimmunity – F7 was a gp120 specific MAb from a BALBc mouse and had VH gene 7183(81X), previously found expressed only in fetal liver [del Real (1999)]

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912 Fab A12 Env(dis) gp41(dis LAI) no HIV-1 infection human(IgG1κ)

References: [Binley (1996)]

- Fab A12: Uncharacterized epitope – variable regions sequenced [Binley (1996)]

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913 Fab A2 Env(dis) gp41(dis LAI) no HIV-1 infection human(IgG1λ)

References: [Binley (1996)]

- Fab A2: Uncharacterized epitope – variable regions sequenced [Binley (1996)]

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914 Fab L9 Env(dis) gp41(dis LAI) no HIV-1 infection human(IgG1κ)

References: [Binley (1996)]

- Fab L9: Uncharacterized epitope – variable regions sequenced [Binley (1996)]

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915 G12 Env( ) gp120(IIIB) Vaccine murine(IgM)

Vaccine: *Vector/type:* chimeric GM-CSF *Strain:* IIIB *HIV component:* gp120

References: [del Real (1999)]

- G12: Murine antibody response to the chimeric construction granulocyte-macrophage colony stimulating factor GM-CSF/gp120 was tested, MAbs from normal mice were gp120 specific, MAbs from nude mice bound gp120 but were polyreactive, and from reconstituted mice were half way between – the anti-gp120 response used a high frequency of VH81X, VHQ52, and VH7183 genes, a family used during fetal life and associated with autoimmunity – G12 was a gp120 from a BALBc reconstructed nude mouse and had VH gene 7183–6 [del Real (1999)]

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916 G2 Env( ) gp120(IIIB) Vaccine murine(IgM)

Vaccine: *Vector/type:* chimeric GM-CSF *Strain:* IIIB *HIV component:* gp120

References: [del Real (1999)]

- G2: Murine antibody response to the chimeric construction granulocyte-macrophage colony stimulating factor GM-CSF/gp120 was tested, MAbs from normal mice were gp120 specific, MAbs from nude mice bound gp120 but were polyreactive, and from reconstituted mice were half way between – the anti-gp120 response used a high frequency of VH81X, VHQ52, and VH7183 genes, a family used during fetal life and associated with autoimmunity – G2 was a gp120 from a BALBc reconstructed nude mouse and had VH gene Q52 [del Real (1999)]

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917 H2 Env(dis) gp41(dis) human(IgMκ)

Donor: BioInvent, Lund, Sweden, commercial

References: [Muller (1991)]

- H2: Anti-idiotypic MAbs (10B3 and 2All) against MAb H2 were generated by immunization of BALBc mice with H2 – they also react with seropositive sera [Muller (1991)]

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918 H8 Env( ) gp120(IIIB) Vaccine murine(IgM)

Vaccine: *Vector/type:* chimeric GM-CSF *Strain:* IIIB *HIV component:* gp120

References: [del Real (1999)]

- H8: Murine antibody response to the chimeric construction granulocyte-macrophage colony stimulating factor GM-CSF/gp120 was tested, MAbs from normal mice were gp120 specific, MAbs from nude mice bound gp120 but were polyreactive, and from reconstituted mice were half way between – the anti-gp120 response used a high frequency of VH81X, VHQ52, and VH7183 genes, a family used during fetal life and associated with autoimmunity – H8 was a gp120 from a BALBc reconstructed nude mouse and had VH gene Q52 [del Real (1999)]

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919 HBW4 Env( ) gp120(IIIB) HIV-1 infection human(IgG1λ)

References: [Moran (1993), Wisnewski (1995), Wisnewski (1996)]

- HBW4: Heavy (V HII) and light (V λII) chain sequenced [Moran (1993)]
- HBW4: HBW4 is V H2 – V-region heavy chain usage was examined and a bias of enhanced V H1 and V H4, and reduced V H3, was noted among HIV infected individuals [Wisnewski (1996)]

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920 K14 Env(dis) gp41(dis) no human(IgG1)

References: [Teeuwsen (1990), Schutten (1995a), Schutten (1995b), Schutten (1996), Schutten (1997)]

- K14: Did not bind to peptides spanning gp41, but it does not react with Env deletion mutant 643–692 – does not react with HIV-2 – competition experiments showed this was an immunodominant conserved epitope in HIV-1 positive sera from Europe and Africa [Teeuwsen (1990)]
- K14: Reduced affinity for both SI and NSI viruses relative to MAb MN215, failed to neutralize SI strain [Schutten (1995b)]
- K14: In a study of NSI and SI virus neutralization, K14 did not influence viral entry [Schutten (1997)]

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921 M25 Env( ) gp41( ) Vaccine murine(IgGκ)

Vaccine: *Vector/type:* purified HIV-1

References: [di Marzo Veronese (1985), Watkins (1996)]

- M25: heavy and light chains cloned and sequenced – binding requires heavy and light chain in combination, in contrast to M77 [Watkins (1996)]

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922 MAG 6B Env(dis) gp120(dis) no Vaccine murine( )

Vaccine: *Vector/type:* sCD4-gp120 complex *Strain:* HXB2 *HIV component:* gp120

Donor: C. Y. Kang, IDEC Inc

References: [Kang (1994)]

- MAG 6B: Amino acid substitutions that reduce binding 10 fold: 256 S/Y, 257 T/R or G or A, 262 N/T, 368 D/R or T, 370 E/R or Q, 381 E/P, 384 Y/E, 421 K/L, 475 M/S, 477 D/V [Kang (1994)]

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923 MO28 Env(dis 632–691) gp41(dis) no *in vitro* stimulation human(IgM)

References: [Ohlin (1989)]

- MO28: This antibody was raised by *in vitro* stimulation with a recombinant Env penv9 – the discontinuous epitope involves hydrophobic regions 632–646, 677–681 and 687–691, proximal to and spanning the transmembrane region – this specificity is unusual in HIV-1 positive sera [Ohlin (1989)]

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924 MO30 Env(dis 632–691) gp41(dis) no *in vitro* stimulation human(IgM)

References: [Ohlin (1989)]

- MO30: This antibody was raised by *in vitro* stimulation with a recombinant Env penv9 – the discontinuous epitope involves hydrophobic regions 632–646, 677–681 and 687–691, proximal to and spanning the transmembrane region – this specificity is unusual in HIV-1 positive sera [Ohlin (1989)]

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925 MO43 Env(dis 632–691) gp41(dis) no *in vitro* stimulation human(IgM)

References: [Ohlin (1989)]

- MO43: This antibody was raised by *in vitro* stimulation with a recombinant Env penv9 – the discontinuous epitope of MO43 involves hydrophobic regions 632–646, 677–681 and 687–691, proximal to and spanning the transmembrane region – this specificity is unusual in HIV-1 positive sera [Ohlin (1989)]

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926 multiple Fabs Env( ) gp120( ) HIV-1 infection human( )

References: [Burton (1991)]

- A panel of anti-gp120 Fabs was generated by antigen selection from a random combinatorial library prepared from bone marrow from an asymptomatic individual [Burton (1991)]

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927 multiple MAbs | Env(dis) | gp120(dis) | | Vaccine | murine( )

Vaccine: *Vector/type:* protein *HIV component:* gp120

References: [Denisova (1996)]

- When gp120 was used as an immunogen, in contrast to gp120 bound to an anti-V3 MAb, few MAbs were generated and all bound better to the native than to the denatured protein – MAbs generated were: G1B12, G2F7, G9G8, G12F12, G1B8, G11F11, G9E8, G1B11, G1B6, G6F2, G2E7 [Denisova (1996)]

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928 multiple MAbs | Env(dis) | gp120(dis) | | Vaccine | murine( )

Vaccine: *Vector/type:* gp120-CD4 complex *HIV component:* gp120

References: [Denisova (1996)]

- When gp120-CD4 was used as an immunogen, in contrast to gp120 bound to an anti-V3 MAb, few MAbs were generated and all bound better to the native than to the denatured protein – MAbs generated were: CG43, CG41, CG49, CG53, CG42, CG4, CG46, CG40, CG52, CG51, CG48, CG50, CG125, CG124, CG121 [Denisova (1996)]

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929 multiple MAbs | Env( ) | gp120( ) | | Vaccine | murine( )

Vaccine: *Vector/type:* protein-Ab complex *HIV component:* gp120 complexed with MAb M77

References: [Denisova (1996)]

- When anti-V3 MAb M77 was bound to gp120 and used as an immunogen, it stimulated many MAbs to linear epitopes, as well as an array of MAbs to discontinuous epitope – 10 of 36 MAbs were mapped to linear epitopes and are mentioned elsewhere in this database, the others are: GV5H1, GV4D5, GV4G10, GV1A8, GV10H5, GV8E11, GV2H4, GV6E6, GV1F7, GV1G9, GV4G5, GV6B12, GV1E8, GV2B7, GV1B11, GV6H5, GV6G2, GV6B5, GV1E10, GV5E3, GV5B9, GV5F4, GV6G4, GV1A12, GV5C11, GV6B6, GV3C10 [Denisova (1996)]

---

930 N2–4 | Env( ) | gp41( ) | no | HIV-1 infection | human(IgG1κ)

Donor: Evan Hersh and Yoh-Ichi Matsumoto

References: [Robinson (1990b)]

- N2–4: No enhancing activity for HIV-1 IIIB [Robinson (1990b)]
- N2–4: NIH AIDS Research and Reference Reagent Program: 528

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931 N70–2.3a | Env(dis 272–509) | gp120(dis) | no | HIV-1 infection | human(IgG1)

Donor: J. Robinson, Tulane University, LA

References: [Robinson (1990a), Takeda (1992)]

- N70–2.3a: Broad reactivity [Robinson (1990a)]
- N70–2.3a: Fc receptor mediated enhancement of HIV-1 infection – binds a conformational site in the carboxyl half of gp120, distinct from 1.5e [Takeda (1992)]

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932 P43110 Env(dis) gp120(dis) ( )

Donor: Advanced Biosciences (Kensington, MD)

References: [di Marzo Veronese (1992), VanCott (1995)]

- P43110: Does not recognized denatured form of the gp120 protein [VanCott (1995)]

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933 P5–3 Env( ) gp120( ) HIV-1 infection human(IgG1λ)

Donor: Evan Hersh and Yoh-Ichi Matsumoto

References: [Robinson (1990b), Pincus (1991)]

- P5–3: No enhancing activity for HIV-1 IIIB [Robinson (1990b)]
- P5–3: Poor immunotoxin activity when coupled to RAC – isotype specified as: IgG3lambda [Pincus (1991)]
- P5–3: NIH AIDS Research and Reference Reagent Program: 378

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934 polyclonal Env( ) Env( ) P and L HIV-1 infection human(IgG3)

References: [Scharf (2001)]

- IgG3: HIVIG was separated into immunologlobulin classes and IgG3 neutralization of HIV strains X4, R5 and X4R5 strains was superior to IgG1 and IgG2, and IgG3 was also a more potent inhibitor of viral fusion – the IgG3 advantage was lost when only Fabs were considered, indicating the IgG3 neutralization efficacy is enhanced due to a longer hinge region of the heavy chain in comparison to IgG1 and IgG2 [Scharf (2001)]

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935 polyclonal Env( ) gp160(IIIB) none HIV-1 infection, Vaccine human( )

Vaccine: *Vector/type:* recombinant protein *Strain:* NL4–3 *HIV component:* gp160 *Stimulatory Agents:* alum

References: [Cox (1999)]

- 60 asymptomatic HIV-1 infected patients were vaccinated with rec gp160 in alum, produced in a baculovirus expression vector in insect cells (VaxSyn), 64 received placebo, and all were followed in a 5 year longitudinal study – a mean of 78% of vaccinated and 82% of those receiving placebo had demonstrable ADCC at the different time intervals in the study, and the vaccine did not enhance ADCC production – patients with rapid and slow disease progression showed similar ADCC levels [Cox (1999)]

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936 polyclonal Env( ) gp160(89.6) yes Vaccine Rhesus macaque( )

Vaccine: *Vector/type:* modified vaccinia Ankara *Strain:* 89.6 *HIV component:* SIVmac239 Gag/Pol and HIV-1 89.6P Env *Stimulatory Agents:* IL2/Ig

References: [Barouch (2001)]

- Four rhesus macaques were vaccinated with a modified vaccinia Ankara (MVA) vaccine that elicited strong CTL responses as well as antibody responses

- The animals were infected when challenged with pathogenic SHIV-89.6P, but had potent CTL responses, secondary NAb responses upon challenge, partial preservation of CD4+ T-cell counts, lower viral loads, and no evidence of disease or mortality by day 168 after challenge – monkeys that got a sham vaccine had high viral load, progressed to disease, and 2/4 were dead by day 168 [Barouch (2001)]

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937 polyclonal Env( ) gp120(SF2) L Vaccine murine, baboon( )

Vaccine: *Vector/type:* recombinant protein *Strain:* SF2 *HIV component:* gp120 *Stimulatory Agents:* PLG+MF59 microparticles

References: [O'Hagan (2000)]

- Microparticles were used as an adjuvant for entrapped HIV-1 gp120 and induced strong serum IgG responses in mice – polylactide co-glycolide polymer (PLG) microparticles in combination with MF59 had the highest response [O'Hagan (2000)]

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938 polyclonal Env( ) gp120(SF2) Vaccine mouse, guinea pig, macaque( )

Vaccine: *Vector/type:* DNA, recombinant protein *Strain:* SF2 *HIV component:* gp120 *Stimulatory Agents:* PLG microparticles, aluminum phosphate, MF-59

References: [O'Hagan (2001)]

- DNA vaccines of codon-optimized Env and Gag genes driven by CMV promotors and absorbed on to PLG microparticles were more effective than naked DNA at eliciting strong Ab responses (more rapid, higher titer, more stable), comparable to gp120 in MF-59 [O'Hagan (2001)]

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939 polyclonal Env( ) gp140(US4) Vaccine mouse, guinea pig, macaque( )

Vaccine: *Vector/type:* DNA *Strain:* US4 *HIV component:* gp140 *Stimulatory Agents:* PLG microparticles, aluminum phosphate, MF-59

References: [O'Hagan (2001)]

- DNA vaccines of codon-optimized Env and Gag genes driven by CMV promotors were absorbed on to PLG microparticles were more effective than naked DNA at eliciting strong Ab responses (more rapid, higher titer, more stable), comparable to gp120 in MF-59 [O'Hagan (2001)]

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940 polyclonal Env( ) gp120( ) L HIV-1 infection chimpanzee(IgG)

References: [Shibata (1999)]

- polyclonal: Purified IgG from chimpanzee sera infected with several HIV-1 strains was used for passive administration to macaques which were subsequently challenged with the virulent SHIV bearing the HIV-1 env DH12 – *in vitro* neutralization correlated with protection *in vivo* [Shibata (1999)]

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941 polyclonal Env( ) gp160(MN) L P HIV-1 infection human(IgA)

References: [Moja (2000)]

- 15 samples isolated from parotid saliva were selected for study of anti-Env IgA – IgA neutralizing activity was detected that was not directed at either EDELKWA or the V3 loop [Moja (2000)]

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942 polyclonal Env( ) Env( ) yes HIV-1 infection human( )

References: [Kim (2001)]

- After HAART reduction of viral load to <400 for three visits over a 12 month interval, 2/11 patients were found to have increased anti-Env Ab binding titers, and neutralizing Abs titers increased against primary isolates US1, and CM237 – no NAB titer increase was seen to more readily neutralized isolate BZ167 – this suggests that in certain individuals the control of HIV-1 by HAART may augment immune control of HIV [Kim (2001)]

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943 polyclonal Env( ) Env( ) yes HIV-1 exposed seronegative human(IgA)

References: [Kaul (2001)]

- Kaul *et al*. provide a concise summary of the findings concerning the presence of Mucosal IgA in highly exposed, uninfected subjects, arguing for a role in protection [Kaul (2001)]

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944 polyclonal Env( ) gp120(SF2) yes Vaccine macaque( )

Vaccine: *Vector/type:* recombinant protein *Strain:* SF2 *HIV component:* gp120, p24 *Stimulatory Agents:* ISCOM

References: [Heeney (1998)]

- The immune responses induced in Rhesus monkeys using two different immunization strategies were studied – one vaccine group was completely protected from challenge infection, the other vaccinees and controls became infected – protected animals had high titers of heterologous NAbs, and HIV-1-specific T helper responses – increases in RANTES, MIP-1α and MIP 1 beta produced by circulating CD8+ T cells were also associated with protection [Heeney (1998)]

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945 polyclonal Env( ) gp120( ) Vaccine macaque( )

Vaccine: *Vector/type:* peptide, recombinant protein *Strain:* SF2, SF33 *HIV component:* gp120 *Stimulatory Agents:* ISCOM, MF59

References: [Verschoor (1999)]

- Attempts were made to broaden immune responses induced in Rhesus monkeys by immunization of animals previously immunized that had resisted homologous challenge, with a second immunization with ISCOM-peptides or a boost with gp120 from SF33 – animals didn't survive a second challenge heterologous challenge virus SHIV(SF33) raising concerns about early antigenic sin [Verschoor (1999)]

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946 polyclonal Env( ) gp120( ) L Vaccine ( )

Vaccine: *Vector/type:* recombinant protein *Strain:* SF2, MN *HIV component:* gp120

References: [McElrath (2000)]

- After 3 immunizations, 210/241 (87%) HIV-1 uninfected vaccinees in a phase II trial developed NAbs – of 140 patients receiving 4 vaccinations, 53% had persistent neutralizing antibodies to homologous virus, and 34% to heterologous virus, measured at day 728 after initial immunization – immunogens were well tolerated– but IVDUs had a decreased Ab response relative to lower risk groups [McElrath (2000)]

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947 polyclonal Env( ) gp120( ) Vaccine murine( )

Vaccine: *Vector/type:* vaccinia *Strain:* IIIB *HIV component:* gp120 *Stimulatory Agents:* GM-CSF/gp120 chimera

References: [Rodriguez (1999)]

- The murine antibody response to a chimeric of granulocyte-macrophage colony stimulating factor GM-CSF/gp120 in vaccinia was not higher titer that the response to a gp120-vaccinia construct, but the breadth of the antibody response was greater [Rodriguez (1999)]
- A cellular response of greater intensity was trigged to the GM-CSF/gp120 vaccinia construct, as measured by prolifeation and gamma IFN production in an Elispot assay

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948 polyclonal Env( ) gp120(YU2) Vaccine murine(IgG)

Vaccine: *Vector/type:* stabilized Env trimer *Strain:* YU2, HXBc2 *HIV component:* Env

Donor: Joseph Sodroski, Harvard Medical School

References: [Yang (2001)]

- Soluble Env trimers were created that were designed to mimic functional Env oligomers – stabilized timers could induce neutralizing antibodies more effectively than gp120, and Abs to the YU2 trimer were cross-reactive within clade B and could neutralize several primary and TCLA reactive strains – the stabilized primers did not neutralize primary isolates outside the B clade, from clades C, D, and E – HXBc2 stabilized trimer antigen elicited strong neutralizing Abs against the homologous isolate HXBc2 TCLA strain, but not against primary isolates [Yang (2001)]

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949 polyclonal Env( ) gp120(MN) Vaccine human( )

Vaccine: *Vector/type:* recombinant protein *Strain:* MN *HIV component:* gp120 *Stimulatory Agents:* QS-21, alum

References: [Evans (2001)]

- Vaccination with QS-21 adjuvant and rsgp120 elicited stronger and more sustained neutralizing antibody responses and lymphocyte proliferation with lower doses of rsgp120 than alum formulations, suggesting QS-21 may be a means to reduce the dose of soluble protein [Evans (2001)]

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950 polyclonal Env( ) gp120( ) yes HIV-1 infection human( )

References: [Binley (2000)]

- HAART inhibited the development of anti-gp120 Ab when initiated during primary infection and sometimes in patients treated within 2 years of HIV-1 infection – HAART during primary infection usually did not inhibit the development of weak NAb responses against autologous virus – 3/4 patients intermittently adherent developed high titers of autologous NAbs, largely coincident with brief viremic periods [Binley (2000)]

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951 polyclonal Env( ) gp120(SIV) yes HIV-1 infection macaque( )

References: [Reitter (1998)]

- This study was not done with HIV-1, but concerned an SIV mutated strain that lacked 4th, 5th and 6th sites for N-linked glycosylation – monkeys infected with the mutant viruses had increased neutralizing activity in their sera relative to monkeys infected with the parental strain

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952 polyclonal Env( ) gp120( ) yes Vaccine human( )

Vaccine: *Vector/type:* recombinant protein *Strain:* SF2 *HIV component:* gp120 *Stimulatory Agents:* MF-59

References: [Nitayaphan (2000)]

- A phase I/II trial was conducted in 52 seronegative Thais immunizing with rgp120 SF2 – the vaccine was safe and 39/40 developed NAb responses to the autologous SF2, while 22/40 were able to cross-neutralize the heterologous strain MN [Nitayaphan (2000)]

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953 polyclonal Env( ) gp120( ) yes Vaccine baboon( )

Vaccine: *Vector/type:* recombinant protein *Strain:* SF2 (subtype B), CM235 (CRF01) *HIV component:* gp120 *Stimulatory Agents:* MF-59

References: [VanCott (1999)]

- Immunization with rgp120 CM235 (CRF01) induced Abs capable of neutralizing TCLA subtype E (CRF01) and subtype B isolates, while rgp120SF2 induced Abs could only neutralize subtype B TCLA isolates – neither immunogen induced Abs capable of neutralizing primary HIV-1 isolates – both rgp120CM235 and rgp120SF2 induced Abs to regions within C1, V1/V2, V3, and C5, but unique responses were induced by rgp120CM235 to epitopes within C2, and by rgp120SF2 to multiple epitopes within C3, V4, and C4 – CM235 baboon sera bound 3- to 12-fold more strongly than the SF2 baboon sera to all subtype E gp120s while binding to subtype B gp120s (except SF2) were within two to threefold for the SF2 and CM235 baboon sera [VanCott (1999)]

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954 polyclonal Env( ) gp120( ) HIV-1 infection human(IgG)

References: [Binley (1997b)]

- Retention of anti-Env antibodies and loss of anti-Gag antibodies during disease progression was studied, and suggested to be the result of the loss of T-cell help and the unique ability of Env to stimulate B cells even in a backdrop of declining CD4 cells, because of the ability of Env to bind to the CD4 molecule [Binley (1997b)]

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955 polyclonal Env( ) gp120(W61D) L Vaccine human( )

Vaccine: *Vector/type:* recombinant protein *Strain:* W61D *HIV component:* gp120

References: [Beddows (1999)]

- rgp120 derived from a R5X4 subtype B virus, HIV-1 W61D, was used to vaccinate healthy volunteers and the resulting sera were compared with HIV-1 positive subjects – vaccinee sera had more potent responses to linear V1/V2 and V3 epitopes than did the sera from HIV-1+ individuals, but could only neutralize homologous or heterologous virus only after adaptation to T-cell lines – neutralization activity was lost after re-adaptation to growth in PBMCs – in contrast, sera from infected individuals could neutralize both PBMC and T-cell line adapted viruses [Beddows (1999)]

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956 polyclonal Env( ) gp120( ) L Vaccine Rhesus macaque( )

Vaccine: *Vector/type:* virus-like particle *HIV component:* Pr55gag, anchored gp120, V3+CD4 linear domains

References: [Wagner (1998)]

- A VLP is a non-infectious virus-like particle self-assembled from HIV Pr55 gag – macaques were immunized with VLPs bound to either gp120 or V3+CD4 linear domains – Gag and Env specific CTL were stimulated in each case, and Ab response to gag and gp120 and was elicited, but the gp120 neutralizing response occurred only with whole gp120, not V3+CD4 – despite the CTL and Ab response, immunized macaques were infected by intervenous challenge with SHIV chimeric challenge stock [Wagner (1998)]

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957 polyclonal Env( ) gp120(IIIB) Vaccine murine( )

Vaccine: *Vector/type:* DNA *HIV component:* gp120, gp160

References: [Shiver (1997)]

- DNA vaccinations of BALBc mice with a gp120 or gp160 DNA vaccine elicited a strong T cell proliferative response with Th1-like secretion of γ interferon and IL-2, with little or no IL-4, as well as antigen specific gp120 Abs [Shiver (1997)]

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958 polyclonal Env( ) gp120( ) L Vaccine murine( )

Vaccine: *Vector/type:* DNA *HIV component:* Gag, Pol, Vif, Env *Stimulatory Agents:* B7, IL-12

References: [Kim (1997)]

- A gag/pol, vif or CMN160 DNA vaccine, when delivered in conjunction with the plasmid encoding the co-stimulatory molecules B7 and IL-12, gave a dramatic increase in both the cytotoxic and proliferative responses in mice
- The Ab response was detected by ELISA, and the CMN160 DNA vaccinated mice also showed a neutralizing Ab response

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959 polyclonal Env( ) gp120( ) P HIV-1 infection human( )

References: [Bradney (1999)]

- Sera were taken from long term non-progressors and evidence for viral escape was noted – serum could neutralize earlier autologous isolates, but not contemporary isolates [Bradney (1999)]

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960 polyclonal Env( ) gp120( ) L P Vaccine human( )

Vaccine: *Vector/type:* canarypox prime with rgp120 boost *Strain:* SF2 *HIV component:* Gag and Env

References: [Belshe (1998)]

- NAbs were obtained by a HIV-1 gag/env in canary pox vaccination of eight volunteers after boosting with rgp120 against lab strains – 1/8 primary isolates was neutralized, BZ167[Belshe (1998)]

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961 polyclonal Env( ) gp120( ) L Vaccine human( )

Vaccine: *Vector/type:* canarypox prime with rgp120 boost *Strain:* LAI, MN, SF2 *HIV component:* Gag, Protease, and gp120 *Stimulatory Agents:* MF-59

References: [Belshe (2001)]

- A phase 2 trial was conducted in 435 volunteers with vCP201, a canary pox vector carrying gp120 (MN in vCP201, and SF2 in the boost), p55 (LAI) and protease (LAI), either alone or with a gp120 boost – NAbs against MN were obtained in 56% of those who received vCP201 alone, and in 94% of those who got the prime with the gp120 boost [Belshe (1998)]

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962 polyclonal Env( ) gp120( ) human(Ig V_H3)
References: [Neshat (2000)]
- HIV-1 gp120 appears to be a B cell superantigen that binds to members of the V_H3 Ig gene family – the gp120 binding site was localized to the Fab portion of the Ab, and discontinuous residues in the V_H region were critical [Neshat (2000)]

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963 polyclonal Env( ) gp120(BH10) Vaccine murine(IgG)
Vaccine: *Vector/type:* DNA *Strain:* ADA, IIIB, 89.6 *HIV component:* gp120 *Stimulatory Agents:* C3d fusion
References: [Ross (2001)]
- gp120 was fused with murine complement protein C3d in a DNA vaccine to enhance the titers of Ab to Env – fusion to C3d resulted in a more rapid onset of Ab response and avidity maturation, after three immunizations in BALB/c mice with DNA on a gold bead delivered with a gene gun, but not in a strong neutralizing Ab response [Ross (2001)]

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964 polyclonal Env( ) gp120( ) none P HIV-1 infection human( )
References: [Sarmati (2001)]
- Some HIV-1 infected patients have increasing CD4 counts despite failing ARV – no correlation was found between NAbs and viral load in these patients [Sarmati (2001)]

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965 polyclonal Env( ) gp120(IIIB) no human(IgM)
References: [Llorente (1999)]
- Combinatorial antibody analysis by phage display and flow cytometry demonstrated that gp120 in HIV-1 negative people is recognized by IgM, but not IgG Abs – IgM Fab reactivity is observed throughout the entire sequence of HIV-1 IIIB gp120 and is characterized by low affinity binding and near germline configuration reflecting a lack of maturation of the IgM repertoire – no neutralizing activity was observed in a non-infected individual before isotope switching [Llorente (1999)]

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966 polyclonal Env( ) gp120(SF2) L Vaccine human(IgM)
Vaccine: *Vector/type:* recombinant protein *Strain:* SF2 *HIV component:* gp120
References: [Locher (1999)]
- High risk voluteers were vaccinated with SF2 gp120 – 3 breakthrough cases were studied – SF2 neutralizing Abs were observed, but Ab titers to autologous virus were never high and took 6 months after HIV-1 infection to develop – viral loads were similar to HIV-1 infected individuals who had not been vaccinated [Locher (1999)]

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967 polyclonal Env( ) gp120(subtypes A-E) yes Vaccine murine(IgG)
Vaccine: *Vector/type:* formaldehyde-fixed whole-cell *HIV component:* gp120
References: [LaCasse (1999), Nunberg(2002)]
- In this study, immunogens were generated that were thought to capture transient envelope-CD4-coreceptor structures that arise during HIV binding and fusion by formaldehyde-fixation of cocultures of cells expressing HIV-1 Env and those expressing CD4 and CCR5 receptors – these cells elicited NAbs in CD4- and CCR5-transgenic mice that neutralized 23/24 primary isolates from clades A-E [LaCasse (1999)]

- A retraction was printed (Science 296:1025, 2002) noting that an unknown cytotoxic effect of these complex sera accounted for a major fraction of the neutralization reported in [LaCasse (1999)] [Nunberg(2002)]

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968 polyclonal Env( ) gp140(IIIB) L Vaccine rabbit(IgG)

Vaccine: *Vector/type:* recombinant protein *Strain:* IIIB *HIV component:* gp140, gp120 *Stimulatory Agents:* MPL-SE adjuvant, QS-21 adjuvant

References: [Earl (2001)]

- Immunization of rabbits with oligomeric gp140 induced production of higher levels of cross-reactive neutralizing Abs than immunization with gp120 – immunization of Rhesus macaques with gp140 yielded strong NAb against IIIB, modest against other lab-adapted strains, and no NAb activity against primary isolates – most neutralizing activity could not be blocked by a V3 peptide – 3/4 vaccinated macaques showed no viral replication upon intravenous challenge with SHIV-HXB2 [Earl (2001)]

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969 polyclonal Env( ) gp140(SF162ΔV2) yes Vaccine rabbit, Rhesus macaque(IgG)

Vaccine: *Vector/type:* DNA, CMV promotor elements *Strain:* SF162, SF162ΔV2 *HIV component:* gp140 *Stimulatory Agents:* MF-59C

References: [Barnett (2001)]

- SF162ΔV2 is a virus that has a 30 amino acid deletion in the V2 loop that does not abrogate its infectivity but renders it highly susceptible to neutralization – when incorporated into a codon-optimized DNA vaccine with a CMV promoter and delivered by gene gun, SF162ΔV2 gave higher neutralizing Ab titers against SF162 than did SF162 itself, and Abs that cross-neutralized non-homologous primary isolates were obtained only when SF162ΔV2, but not intact SF162, was used as the immunogen – Control MAbs 2F5 and 2G12 could neutralize all of the following primary isolates: 91US056(R5), 92US714(R5), 92US660(R5), 92HT593(R5X4), and BZ167(R5X4), while after the first protein boost, the sera from two SF162ΔV2 immunized macaques could neutralize 91US056(R5), 92US714(R5), 92US660(R5) and ADA(R5), but not 92HT593(R5X4) or 92US657(R5) – the pattern of cross-recognition shifted after the second boost [Barnett (2001)]

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970 polyclonal Env( ) gp120(SF162ΔV2) Vaccine Rhesus macaque( )

Vaccine: *Vector/type:* DNA prime with recombinant protein boost *Strain:* SF162ΔV2 *HIV component:* gp140 *Stimulatory Agents:* MF-59C

References: [Cherpelis (2001b), Cherpelis (2001a)]

- Two animals were immunized both intradermally and intramuscularly at weeks 0, 4, and 8 with a codon optimized DNA vector expressing the SF162V2 gp140 envelope with an intact gp120-gp41 cleavage site, and both developed lymphoproliferative responses and potent neutralizing Abs – CD8+ T lymphocytes were depleted in the animals and they were challenged with SHIV162P4 – at peak viremia, plasma viral levels in the vaccinated animals were 1 to 4 logs lower than those in the unvaccinated animals [Cherpelis (2001b)]

- HIV-1 SF162ΔV2 gp140 envelope was used in a DNA-prime plus protein-boost vaccination methodology in Rhesus macaques, the animals were depleted of their CD8+ T lymphocytes, and challenged with pathogenic SHIV(SF162P4) – the vaccinated macaques had lower peak viremia, rapidly cleared virus from the periphery, and developed delayed seroconversion to SIV core antigens relative to non-vaccinated controls [Cherpelis (2001a)]

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971 polyclonal Env( ) gp160( ) no HIV-1 infection human( )

References: [Ahmad (2001)]

- High CD4+ T-cell count and low viral load was correlated with high ADCC anti-HIV-1 Env Ab titers in a study of 46 HIV-1 infected individuals from all disease stages [Ahmad (2001)]

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972 polyclonal Env(dis) gp160(dis) P HIV-1 infection human(IgG)

References: [Beirnaert (2001)]

- Neutralizing antibodies are thought to inhibit HIV entry by blocking either binding or fusion – six broadly cross-neutralizing sera that can neutralize group M and O viruses inhibit the binding to PBMCs – the nine primary isolates tested in this study represented very diverse subtypes and recombinant forms, and different co-receptor usage [Beirnaert (2001)]

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973 polyclonal Env(dis) gp160(dis) P HIV-1 infection human(IgG)

References: [Beirnaert (2000)]

- Sera from 66 HIV individuals from diverse geographic locations could neutralize primary isolates to different extents: broad cross-neutralizing isolates could neutralize 14 primary isolates from HIV-1 group M clades A-H and three O isolates, limited cross-neutralizing sera neutralized some isolates, and non-neutralizing sera – 6/7 broadly neutralizing sera, were from African women despite only 14/66 study subjects being women – ability to neutralize three key isolates, MNlab (envB/gagB, X4 coreceptor), VI525 (envG/gagH, envA/gagA, R5X4) and CA9 (Group O, R5) was predictive of being able to neutralize an additional set of 14 primary isolates [Beirnaert (2000)]

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974 polyclonal Env( ) gp41(539–684 BH10) Vaccine murine(IgG)

Vaccine: *Vector/type:* recombinant protein *HIV component:* gp41

References: [Bai (2000)]

- Murine rsgp41 antisera recognized a common epitope on human IFN-α (aa 29–35 and aa 123–140) and on human IFN-β (aa 31–37 and aa 125–142), suggesting that elevated levels of Ab to IFNs found in HIV+ individuals may be due to a cross-reactive gp41 response [Bai (2000)]

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975 polyclonal Env( ) gp41(539–684 BH10) Vaccine murine(IgG)

Vaccine: *Vector/type:* recombinant protein *HIV component:* gp41

References: [Bai (2000)]

- There is a common epitope in HIV-1 gp41, and IFNalpha and IFNbeta

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976 T20 Env(dis) gp120(dis IIIB) no Vaccine murine(IgG)

Vaccine: *Vector/type:* vaccinia *Strain:* IIIB *HIV component:* oligomeric gp140

Donor: P. Earl, National Institute of Allergy and Infectious Diseases, NIH, Bethesda, MD
References: [Earl (1994), Otteken (1996), Sugiura (1999)]

- T20: Pulse label experiments of 4 MAbs (D20, D27, T20, and T22) binding to noncleavable gp140 revealed that these anti-CD4BS MAbs bound with a delay, and that the epitope formed with a $t_{1/2}$ of about 10 minutes [Otteken (1996)]
- T20: A comparison of 25 gp120 specific, conformation dependent MAbs was done – T20 is part of a group of MAbs labeled AII – all AII MAbs were broadly cross-reactive with gp160 from B-clade R5, X4, and R5X4 viruses, and could only partially block CD4 binding [Sugiura (1999)]

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977 T27 Env(dis) gp120(dis IIIB) no Vaccine murine(IgG)

Vaccine: *Vector/type:* vaccinia *Strain:* IIIB *HIV component:* oligomeric gp140

Donor: P. Earl, National Institute of Allergy and Infectious Diseases, NIH, Bethesda, MD
References: [Earl (1994), Sugiura (1999)]

- T27: A comparison of 25 gp120 specific, conformation dependent MAbs was done – T27 is part of a group of MAbs labeled AII – all AII MAbs were broadly cross-reactive with gp160 from B-clade R5, X4, and R5X4 viruses, and could only partially block CD4 binding [Sugiura (1999)]

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978 T3 Env(dis) gp41(dis HXB2) Vaccine murine(IgG)

Vaccine: *Vector/type:* tetrameric Env *HIV component:* Env

References: [Earl (1994), Earl (1997), Zwick (2001b)]

- T3: Partially conformation dependent – doesn‘t bind to short peptides, but does bind to the region spanning 641–683 – binding can be blocked by MAbs D43, D38 and D45 – MAbs in this competition group reacted with 9/10 HIV-1 strains, not binding to JRFL [Earl (1997)]
- T3: T3 partially competes with MAb Z13, but not MAb 4E10, both of which bind to gp41 proximally to the 2F5 epitope and have a broad neutralizing potential [Zwick (2001b)]

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979 T30 Env(dis) gp41(dis) no Vaccine murine( )

Vaccine: *Vector/type:* tetrameric Env *HIV component:* Env

References: [Earl (1994), Earl (1997)]

- T30: Binds in the region 580 to 640, but does not bind to peptides spanning this region – binding depends on N-linked glycosylation of Asn 616 – no other antibody tested inhibited binding, but binding could be inhibited by sera from HIV+ individuals [Earl (1997)]

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980 T4 Env(dis) gp41(dis IIIB) L Vaccine murine(IgG)

Vaccine: *Vector/type:* vaccinia *Strain:* IIIB *HIV component:* oligomeric gp140

References: [Earl (1994), Broder (1994), Richardson (1996), Weissenhorn (1996), Earl (1997), Otteken (1996), Binley (1999), Stamatatos (2000), Srivastava (2002)]

- T4: one of five MAbs (T4, T6, T9, T10 and T35) in a competition group that bind to a conformation-dependent epitope in gp41 and is oligomer specific – neutralizes IIIB and SF2 [Broder (1994)]
- T4: Does not bind to soluble monomeric gp41(21–166) that lacks the fusion peptide and membrane anchor, only to the oligomer gp140, as does T6 [Weissenhorn (1996)]
- T4: This antibody, along with 7 others (M10, D41, D54, T6, T9, T10 and T35), can block the linear murine MAb D61, and the human MAb 246-D, which both bind to the immunodominant region near the two Cys in gp41 – most of these antibodies are oligomer dependent – all of the MAbs are reactive with ten different HIV-1 strains – members of this competition group are blocked by sera from HIV-1+ individuals [Earl (1997)]
- T4: MAbs T4 and T6 bind only to oligomer, and pulse chase experiments indicate that the epitope is very slow to form, requiring one to two hours [Otteken (1996)]
- T4: The MAbs with the broadest neutralizing activity, IgG1b12, 2G12 and 2F5, all have high affinity for the native trimer, indicating that they were raised in an immune response to the oligomer on the virion surface rather than dissociated subunits – a disulfide linked gp120-gp41 (SOS gp140) was created to mimic the native conformation of Env and explore its potential as an immunogen – SOS gp140 is recognized by NAbs IgG1b12, 2G12, and CD4-IgG2, and also by anti-V3 MAbs 19b and 83.1 – SOSgp140 is not recognized by C4 region MAbs that neutralize only TCLA strains, G3-42 and G3-519 – nor did it bind C11, 23A, and M90, MAbs that bind to gp120 C1 and C5, where it interacts with gp41 – MAbs that bind CD4 inducible epitopes, 17b and A32 were very strongly induced by CD4 in SOS gp140 – anti-gp41 MAbs that bind in the region that interacts with gp120, 7B2, 2.2B, T4, T15G1 and 4D4, did not bind to SOSgp140, in contrast to 2F5, which binds to the only gp41 epitope that is well exposed in native gp120-gp41 complexes [Binley (1999)]
- T4: Soluble gp140 derived from SF162, a neutralization-resistant primary isolate, and SF162AV2 a neutralization-susceptible isolate with 30 amino acids deleted from the V2 loop, were generated with or without the gp120-gp41 cleavage site intact – all forms are recognized by oligomer-specific MAb T4 and show enhanced binding of CD4i MAb 17b when sCD4 is bound – the fused forms are less efficiently recognized than the cleaved forms by polyclonal neutralizing sera from HIV-infected patients – the V3 loop is more exposed on the fused form [Stamatatos (2000)]
- T4: Oligomeric gp140 (o-gp140) derived from R5 primary isolate US4 was characterized for use as a vaccine reagent – antigen capture ELISA was used to compare the antigenicity of gp120 and o-gp140 using a panel of well characterized MAbs – T4 recognized o-gp140 [Srivastava (2002)]